Harvard Journal of Law & Technology
Volume 15, Number 1 Fall 2001
PAGE LAYOUT AND NUMBERING DO NOT CORRESPOND TO ORIGINAL

FDA REGULATION OF HUMAN CLONING: USURPATION OR STATESMANSHIP?

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I. INTRODUCTION

In February of 1997, *The Observer* of London reported that a team of researchers at the Roslin Institute in Scotland had successfully "cloned" a sheep, which they named Dolly.[1] The research team, led by Dr. Ian Wilmut, achieved this breakthrough in genetic technology through the use of a technique called somatic cell nuclear transfer.[2] In simple terms, somatic cell nuclear transfer involves extracting the genetic material from a cell of a donor and injecting it into another cell that has been emptied of its own genetic material, resulting in an "embryo" that is a genetic clone of the original donor organism.[3] The successful use of this technique to produce a living mammal represented a major scientific breakthrough, but it also raised fears that humans could be cloned using similar means.[4]

Within weeks of the report of Dolly's birth, President Clinton imposed an administrative ban on federal funding of attempts to clone human beings[5] and simultaneously asked the National Bioethics Advisory Commission ("NBAC") to address the legal, moral, and ethical

1. *See* Robin McKie, *Scientists Clone Adult Sheep*, THE OBSERVER (London), Feb. 23, 1997, at Al.

2. *See* I. Wilmut et al., *Viable Offspring Derived from Fetal and Adult Mammalian Cells*, 385 NATURE 810 (1997).

3. *See id.*

4. *See* Frank Bruni, *Experts Urge No Hasty Curbs on Cloning*, N.Y. TIMES, Mar. 14, 1997, at B2; Declan Butler & Meredith Wadman, *Calls for Cloning Ban Sell Science Short*, 386 NATURE 8 (1997); *Cloning for Good or Evil*, N.Y. TIMES, Feb. 25, 1997, at A26; Nancy J. Duff, *Clone with Caution: Don't Take Playing God Lightly*, WASH. POST, Mar. 2, 1997, at C1; Jane Gross, *Thinking Twice About Cloning*, N.Y. TIMES, Feb. 27, 1997, at B1; Robert Langreth, *Cloning Has Fascinating, Disturbing Potential*, WALL ST. J., Feb. 24, 1997, at B1; *One Lamb, Much Fuss*, 349 LANCET 661 (1997); *To Clone or Not to Clone?*, 114 CHRISTIAN CENTURY 286 (1997); Rick Weiss, *Lost in the Search for a Wolf Are Benefits in Sheep's Cloning*, WASH. POST, Mar. 3, 1997, at A3; George F. Will, *The Moral Hazards of Scientific Wonders*, WASH. POST, Feb. 25, 1997, at A17; Nigel Williams, *Cloning Sparks Calls for New Laws*, 275 SCI. 1415 (1997); Kenneth L. Woodward, *Today the Sheep . . . Tomorrow the Shepherd? Before Science Gets There, Ethicists Want Some Hard Questions Asked and Answered*, NEWSWEEK, Mar. 10, 1997, at 60; Robert Wright, *Can Souls Be Xeroxed?*, TIME, Mar. 10, 1997, at 73.

5. *See Memorandum on the Prohibition on Federal Funding for Cloning of Human Beings*, 33 WKLY. COMP. PRES. DOC. 281 (1997).

issues surrounding cloning technology.[6] The President also proposed enactment of the Cloning Prohibition Act of 1997,[7] a bill that specifically sought to ban the creation of human beings using somatic cell nuclear transfer. However, this bill made no progress in Congress.

While the Clinton Administration's bill was before lawmakers, several proposed their own bills targeted at experiments that could result in the cloning of a human being.[8] When Chicago physicist Dr. Richard Seed announced his plan to clone a human being,[9] the public controversy intensified, and legislative efforts to restrict the use of cloning technology increased.[10] Despite intense interest in anti-cloning legislation, however, Congress was unable to agree on the details of any particular proposal. This stalemate was due in part to the lobbying efforts of doctors and scientists who feared the potential impact of legislation on accepted and widely-used procedures.[11]

Without waiting for congressional action, and possibly to forestall extreme legislation, the Food and Drug Administration ("FDA") abruptly declared that it already possessed, and was prepared to exercise, authority to regulate cloning experiments. The Agency's announcement took an unusual form. Dr. Michael Friedman, the FDA's Acting Commissioner, asserted the Agency's jurisdiction in response to a question posed by the moderator of a popular public radio call-in show, but his remarks were not immediately memorialized in writing.[12] Several months later, on October 26, 1998, the FDA reiterated this position, invoking both the Federal Food, Drug, and Cosmetic Act ("FDCA")[13] and the Public Health Service Act ("PHSA").[14] This statement took the form of a "Dear Colleague" letter by Dr. Stuart Nightingale, Associate Commissioner, to institutional review boards

6. *See Clinton Urges Ban on Cloning of Humans*, 114 CHRISTIAN CENTURY 583 (1997).

7. *See id.*

8. *See* Diane M. Gianelli, *Congress Weighs Ban on Cloning: Bills Differ on Research Issues*, AM. MED. NEWS, Feb. 23, 1998, at 3; Lisa Seachrist, *Armey Wants Cloning Bill on Floor by Memorial Day*, BIOWORLD TODAY, Apr. 29, 1998, at 1; Lisa Seachrist, *Feinstein, Kennedy Offer Bill to Ban Human Cloning*, BIOWORLD TODAY, Feb. 3, 1998, at 1.

9. *See* J. Madeleine Nash, *Cloning's Kevorkian: Who is This Eccentric Physicist Named Seed Who Wants to Start a Clinic in Chicago to Clone Humans?*, TIME, Jan. 19, 1998, at 58.

10. *See* Gianelli, *supra* note 8, at 3.

11. *See id.*

12. *See* Rick Weiss, *Human Cloning Will Be Regulated: FDA Asserts It Has Statutory Authority to Regulate Attempts at Human Cloning*, WASH. POST, Jan. 20, 1998, at A1.

13. *See* 21 U.S.C. §§ 301–97 (2000).

14. *See* 42 U.S.C. §§ 20–30 (2000).

("IRBs") throughout the country.[15] Dr. Nightingale's letter provided a somewhat clearer picture of the FDA's legal theory. Dr. Nightingale explained that any experiment using cloning research to create a human being was subject to the FDCA's investigational new drug requirements and could only be undertaken after Agency approval of an investigational new drug ("IND") application.[16] More recently, the FDA reaffirmed its position that existing laws give it authority to regulate and prohibit experiments designed to clone human beings. This time the Agency spoke directly to Congress in testimony by Dr. Kathryn Zoon, the Director of the FDA's Center for Biologics Evaluation and Research.[17]

In June of 2001, members of Congress and the Bush Administration entered into serious discussions to develop legislation aimed at human cloning research.[18] Claude A. Allen, the Deputy Director for Health and Human Services ("HHS"), stated that the Bush Administration would prefer a broad legislative ban on human cloning research and thus supports a bill that would make it a crime for anyone to create a cloned human embryo for any purpose.[19] Opponents of this position favor narrower legislation that would allow scientists to clone human embryos for research purposes, provided that they did not "intend" to develop those embryos into human babies.[20] The disagreement between those who oppose all cloning and those who fear the impact of a broad ban on medical research continues to inhibit the passage of human cloning legislation.[21]

The FDA's claims of jurisdiction over human cloning have nonetheless created a de facto, if possibly hollow, regulatory regime. Rather than a thoughtful strategy for meeting a novel regulatory challenge, the Agency's repeated assertions apparently represent a response to public and congressional demands concerning cloning.

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15. *See* Dr. Stuart Nightingale, Dear Colleague Letter About Human Cloning, Oct. 26, 1998, *at* http://www.fda.gov/oc/oha/irbletr.html [hereinafter Nightingale Letter] (asserting that the FDA "has jurisdiction over clinical research using cloning technology to create a human being" under the PHSA and the FDCA, and informing "IRBs of the regulatory process that is required before an investigator can proceed with such a clinical investigation").

16. *See id*.

17. *See Issues Raised by Human Cloning Research: Hearing Before the Subcomm. on Oversight and Investigations of the House Comm. on Energy and Commerce*, 107th Cong. 78–81 (2001), *available at* http://energycommerce.house.gov/107/hearings/03282001Hearing141/Zoon205.htm (statement of Dr. Kathryn Zoon, Director, Center for Biologics Evaluation and Research, FDA) [hereinafter Zoon Testimony].

18. *See* Rick Weiss, *Bush Backs Broad Ban on Human Cloning*,WASH. POST, June 21, 2001, at A1.

19. *See id*.

20. *See id.*

21. *See generally id.*

However, the plausibility and propriety of the FDA's claim remain important issues because both the Clinton and Bush Administrations and Congress have failed to develop any such strategy. In the absence of targeted legislation, the FDA's program for regulating clinical studies of new medicines will be the instrument that enables the federal government to oversee research into cloning and cloning-related technologies. The specific elements of the FDA's regulatory regime will grow in importance as cloning research accelerates. Recent experiments using cattle have produced living clones,[22] while research involving primates presents the prospect of human cloning in a way that even Dolly did not. Such breakthroughs keep the issue of cloning before the public and exert continuing pressure on government officials and existing regulatory regimes.

This Article examines the legal and policy issues surrounding the FDA's asserted jurisdiction over attempts to clone a human being. It concludes that the FDA's facial authority to regulate some applications of cloning technology and, in particular, experiments designed to produce a human being might be upheld if challenged. The Article also suggests, however, that there are legitimate grounds to question the procedure through which the Agency has sought to establish its regulatory jurisdiction. Finally, it argues that the Agency's procedural shortcut has deflected public debate about the formulation of societal limits on this promising and provocative technology.

Part II of the Article sketches out the science behind cloning and the development of cloning technology, providing context for the public debate on cloning and our discussion of regulatory possibilities. Part III recounts the FDA's assertion of regulatory authority and examines the possible legal bases for its jurisdiction. Part IV explores procedural objections to the FDA's position, including possible claims that the Agency has violated the Administrative Procedure Act ("APA").[23] Part V examines whether administrative regulation is a normatively attractive means of addressing the complex scientific, moral and ethical issues surrounding cloning. The Article concludes by examining other models of societal decision-making that could address the concerns that originally prompted calls to prohibit human cloning.

22. *See* Gina Kolata, *On Cloning Humans, 'Never' Turns Swiftly Into 'Why Not'*, N.Y. TIMES, Dec. 2, 1997, at A1.

23. Administrative Procedure Act, 5 U.S.C. §§ 500–04, 551–59, 561–84, 591–96 (2000).

II. THE EVOLUTION OF GENETIC TECHNOLOGY AND THE SCIENCE OF CLONING

The public debate over cloning technology generally, and the possibility of cloning a human being in particular, has lacked neither fervor nor imagination. The emotional nature of the topic and the complexity of the science, however, have inhibited informed public dialogue. Too often, this debate has proceeded without a real grasp of the underlying science or an appreciation of cloning's potential benefits and dangers. While these limitations are often present when cutting-edge science attracts widespread popular interest, such an impoverished exchange is unlikely to provide the basis for a wise public policy.

The lack of understanding of human cloning has been particularly disconcerting in the legislative arena. A bill prohibiting human cloning was withdrawn in Florida, largely due to its authors' failure to craft a law distinguishing cloning from other valuable and accepted forms of genetic technology.[24] Other legislative efforts to prohibit attempts to clone a human being have been similarly over-inclusive or, conversely, have failed to restrict the very experiments at which they were aimed.[25] Such misunderstandings in both public discourse and legislative deliberation challenge serious attempts to fashion appropriate regulation.

To provide a basis for evaluating the present default approach, this Part first describes the science behind human cloning. It begins with a working definition of cloning and illustrates some of its present applications and future possibilities in a variety of fields. It then traces the historical development of genetic technology and the science of cloning to the conclusion that human cloning is a real possibility.

A. Cloning Techniques: Definitions and the Problem of Context

Cloning has been defined in various ways. For example, *Webster's Dictionary* defines cloning as the creation of "the aggregate of the asexually produced progeny of an individual whether natural . . . or otherwise."[26] Alternatively, the NBAC has described cloning as the production of "a precise genetic copy of a molecule, cell, plant, animal, or human being."[27] The breadth of these definitions points to one of the

24. *See* Meredith Wadman, *Cloning Without Human Clones*, WALL ST. J., Jan. 20, 1998, at A18.

25. *See generally* Katharine Q. Seelye, *G.O.P. Lawmaker Proposes Bill to Ban Human Cloning*, N.Y. TIMES, Mar. 6, 1997, at B12.

26. WEBSTER'S THIRD NEW INTERNATIONAL DICTIONARY 426 (1993).

27. CLONING HUMAN BEINGS: REPORT AND RECOMMENDATIONS OF THE NATIONAL BIOETHICS ADVISORY COMMISSION, National Bioethics Advisory Commission 13 (1997), *at* http://bioethics.gov/pubs/cloning1/cloning.pdf [hereinafter NBAC REPORT].

central problems in the legal and ethical debates over cloning: the term encompasses a wide variety of activities, processes, and techniques. Use of the term without including at least some context is at best unhelpful and at worst misleading. It is therefore useful to review some of the more common kinds of natural and artificial cloning and cloning techniques.

Although this Article, and current public debate generally, focus on experimentally-induced methods of cloning, cloning is a process that occurs regularly in nature.[28] Humans can mimic such natural cloning by taking advantage of a plant's ability to generate an entirely new organism from only a portion of the original. Thus, every time a gardener makes a cutting from a houseplant that can grow into an adult tree, reproduction occurs through an asexual process, and cloning is achieved.[29] This ability of plants to clone themselves has proved useful in agriculture, where cloning technologies are frequently used to achieve product uniformity, improved productivity, and the reproduction of disease-resistant strains.[30]

The use of cloning technology has become as routine in the laboratory as it is in the agricultural setting. In the process known as molecular cloning, scientists produce identical copies of deoxyribonucleic acid ("DNA"), the basic building block of genes.[31] They do so by copying DNA fragments and then amplifying them, or "growing" them, in a host cell.[32] This technique is valuable because the existence of a great number of identical DNA strands expands the ability of researchers to conduct scientific experiments using DNA.[33] Molecular cloning is used in routine DNA testing as well as in various medical experiments. In fact, experiments using cloned DNA have been responsible for the discovery of ways to produce valuable medicines like insulin, which is used to treat diabetes, and the protein alpha-1 antitrypsin ("AAT"), which can be used to treat emphysema.[34]

Cloning technology is also commonplace at the cellular level, where laboratory scientists make copies of cells derived from the same *soma*, or body, by growing these cells in a culture.[35] The resulting production cell lines are a valuable source of raw material for experiments because

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28. *See id.* at 14 (stating that "genetically identical copies of whole organisms are commonplace in the plant breeding world and are commonly referred to as *'varieties'* rather than *'clones'*") (emphasis added).

29. *See* ROBERT G. MCKINNELL, CLONING: A BIOLOGIST REPORTS 6–8 (1979).

30. *See* OFFICE OF TECHNOLOGY ASSESSMENT, GENETIC TECHNOLOGY: A NEW FRONTIER 137–40 (1982).

31. *See* NBAC REPORT, *supra* note 27, at 13–14.

32. *See id.*

33. *See id.*

34. *See* JOHN C. AVISE, THE GENETIC GODS 172–84 (1998).

35. *See* NBAC REPORT, *supra* note 27, at 14.

they provide scientists with a large supply of genetically identical cells. Researchers can then conduct experiments without fear of depleting the available genetic material. Thus, cellular cloning techniques are useful in developing and testing new medicines.[36] Because neither cellular nor molecular cloning uses germ cells (eggs or sperm), the cloned cells are not biologically capable of developing into a living organism. These techniques therefore do not present the possibility of using cloning to produce a human being.

Some forms of animal cloning, less sophisticated than the technique used to produce Dolly, are used frequently in the livestock industry.[37] In a method called blastomere separation, scientists split developing embryos into several cells while those cells are still totipotent, meaning that each cell still possesses the potential to develop into an entirely new organism.[38] These totipotent cells can then be grown into genetically identical animals. This technique has been used to duplicate animals with desirable traits and to create small herds of "genetic carbon-copy cows" with beneficial attributes.[39] There has also been speculation that the ability to create designer animals might lead to great advances in medicine because these animals could yield medicines to treat disease or to provide organs for transplant.

In the complex form of animal cloning now known as nuclear transplantation cloning or nuclear transfer technology, scientists remove the haploid nucleus of an egg and replace it with the diploid nucleus of a somatic cell.[40] The egg cell can then be grown into an animal whose genes come from only one "parent."[41] This technique is promising for the livestock industry because, like blastomere separation, nuclear transfer would allow the creation of genetic copies of animals with particularly desirable traits.[42] Although nuclear transfer technology is not unknown in the livestock industry, this science is not yet cost-effective.[43] Nevertheless, this technique also holds great promise for livestock production and, potentially, for advances in human medicine.[44]

This necessarily brief survey demonstrates that all broad definitions of cloning will be imprecise. Any discussion about the propriety of

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36. *See id.* at 26.
37. *See id.* at 37.
38. A more technical definition of "totipotency" is "[t]he capacity retained by some cells to differentiate and proliferate into the diverse cell types of an adult organism." AVISE, *supra* note 34, at 273.
39. *See id.* at 185.
40. *See* NBAC REPORT, *supra* note 27, at 14–16.
41. *See id*.
42. *See* AVISE, *supra* note 34, at 185.
43. *See* Justin Gillis, *Cloned Cows Are Fetching Big Bucks*, WASH. POST, Mar. 25, 2001, at A1.
44. *See id*.

"cloning" should therefore identify both the type of technique being contemplated and the ends to which that technique is directed. The recent debate over government regulation has focused on technologies that might be used to clone a human being. However, many cloning techniques are already widely accepted for both scientific and industrial purposes. Indeed, the ability to clone organisms using nuclear cell transfer has a relatively long history. Dr. Wilmut's breakthrough may have raised the specter of human clones for the first time, but his achievement was in reality just one more step in the accelerating progression of genetic technology.

B. The Development of Cloning Technology

The rapid advance of cloning technology is a relatively recent phenomenon. Most early cloning experiments struggled with the problem of cell differentiation. Cell differentiation is "the process by which . . . specialized cells, tissues, and organs are formed . . . during the development of the individual from fertilized ovum."[45] Cell differentiation is therefore a central step in the process by which single cells grow into complete organisms. The human body is made up of many different kinds of cells. A liver cell, for example, is different from a skin cell.[46] If cell differentiation did not occur, the cells which make up specialized parts of the human body could not form, and the resulting mass of unspecialized cells would be incapable of developing into a whole organism. Differentiation presents the central challenge for cloning research.

In the development of successful cloning technology, the key element of cell differentiation is the genetic alteration of cells as they differentiate. The implications of this genetic transformation are significant: because living organisms initially develop from unspecialized cells, scientists cannot successfully clone an organism without recreating unspecialized cells. However, because researchers can only work with genetic material drawn from specialized cells, they must first transform specialized cells into unspecialized cells. Without some means of reversing the process of differentiation, scientists would not be able to produce a clone from adult cells.

The original breakthrough in the use of nuclear transplantation cloning came in 1952 when Robert Briggs and Thomas J. King used the technique to clone a frog.[47] In these landmark experiments, Briggs and

45. HENRY HARRIS, NUCLEUS AND CYTOPLASM 142 (3d ed. 1974).

46. *See id*.

47. *See* Robert Briggs & Thomas J. King, *Transplantation of Living Nuclei from Blastula Cells into Enucleated Frogs' Eggs*, 38 PROC. NAT'L. ACAD. SCI. 455 (1952); *see also* ROBERT G. MCKINNELL, CLONING: OF FROGS, MICE AND OTHER ANIMALS (2d ed.

King injected the nucleus of a donor cell, drawn from a frog embryo, into an egg whose own nucleus had been inactivated.[48] The resulting cells were genetic copies of the donor frogs.[49] While these early experiments succeeded in producing viable embryos, the resulting clones never developed beyond the tadpole stage.[50] Nevertheless, these experiments were important for two reasons. First, they showed that cells remain totipotent even after the initial cell divisions. Second, the experiments proved that specialized cells are capable of producing viable embryos.

Researchers extended the work of Briggs and King to a variety of amphibious creatures, including several species of toads, frogs, and salamanders. They also also broadened the types of cells used, transferring the nuclei of such diverse types of adult cells as white blood cells,[51] red blood cells,[52] skin cells,[53] sperm cells,[54] and kidney tumor cells.[55] In one of the most important experiments, J.B. Gurdon demonstrated that nuclear transfer from an adult cell could produce tadpoles.[56] Although this experiment failed to produce a normal adult frog,[57] it was a very important development on the road to Dolly, showing that it might be possible to "reprogram" adult cells and thereby reverse the process of cell differentiation.

The first efforts to use nuclear transfer techniques to clone mammals involved experiments on mice.[58] These initial attempts to clone mice were similar to those involving frogs: the DNA from a cell in the early stages of development was taken and injected into an egg cell.[59]

1985) (offering an accessible account of this experiment and other early research done in the area of genetic cloning).

48. *See* Briggs & King, *supra* note 47, at 456–57.

49. *See id*.

50. *See id.* at 457.

51. *See* L. Du Pasquier & M.R. Wabl, *Transplantation of Nuclei for Lymphocytes of Adult Frogs into Enucleated Eggs: Special Focus on Technical Parameters*, 8 DIFFERENTIATION 9 (1977).

52. *See* Rudolf B. Brun, *Developmental Capacities of Xenopus Eggs, Provided with Erythrocyte or Erythroblast Nuclei from Adults*, 65 DEV. BIOLOGY 271 (1978).

53. *See* J.B. Gurdon et al., *The Developmental Capacity of Nuclei Transplanted from Keratinized Cells of Adult Frogs*, 34 J. EMBRYOL. EXP. MORPHOL. 93 (1975).

54. *See* M.A. Di Berardmo & N.J. Hoffner, *Development and Chromosomal Constitution of Nuclear Transplants Derived from Male Germ Cells*, 176 J. EXP. ZOOL. 61 (1971).

55. *See* Robert G. McKinnell, *The Pluripotential Genome of the Frog Renal Tumor Cell as Revealed by Nuclear Transplantation*, 9 INT'L. REV. CYTOLOGY SUPPLEMENT 179 (1979).

56. *See* J.B. GURDON, THE CONTROL OF GENE EXPRESSION IN ANIMAL DEVELOPMENT 18 (1974).

57. *See id.* at 23.

58. *See* MCKINNELL, *supra* note 47, at 77.

59. *See id*.

Scientists then tried to grow these cells into a population of genetic copies.[60] Early experiments were unsuccessful, but by the 1980s, researchers began to enjoy a great deal of success producing fertilized eggs from embryonic cells.[61] Even in these experiments, however, once the fertilized egg proceeded beyond the two-cell division stage, success rates declined.[62]

In recent years, as scientists have continued to push on the limits of what was once thought possible, these tentative successes with mice have been dramatically expanded. Nuclear transfers are being done in mice as late as the eight-cell stage, and significantly later transfers have been accomplished with rabbits (thirty-two- to sixty-four-cell stage) and in cows and sheep (120-cell blastocyte stage).[63] These developments are startling, surpassing what most researchers would have predicted a decade ago. Even so, researchers had not yet been able to produce a viable embryo from an adult cell. At least until Dolly.

C. The Science Behind Dolly and the Twenty-Two Mice

The Roslin Institute's creation of Dolly was not remarkable because it involved cloning. By 1997, the work of Briggs and King was four and a half decades old, and genetic researchers had continued to expand the possibilities of cloning through numerous technological innovations.[64] In fact, the Roslin Institute had previously reported the birth of live lambs from embryonic cells.[65] Yet scientists remained skeptical about the possibility of cloning a viable embryo from an adult cell. It was this achievement that made the announcement of Dolly's arrival so stunning. The Roslin Institute's team had managed to create, not just a viable embryo, but a live sheep, using the genetic material from an adult cell.

The Roslin scientists began by removing mammary gland cells (cells from the udder) from a Finn Dorset ewe.[66] They then grew these cells in a tissue culture.[67] While being grown, the mammary gland cells were "starved" of important nutrients until they entered a state of

60. *See id*.

61. For accounts of the most successful of these experiments, see James McGrath & Davor Solter, *Inability of Mouse Blastomere Nuclei Transferred to Enucleated Zygotes to Support Development In Vitro*, 226 SCI. 1317 (1984); James McGrath & Davor Solter, *Maternal T^{hp} Lethality in the Mouse is a Nuclear, Not Cytoplasmic, Defect*, 308 NATURE 550 (1984); James McGrath & Davor Solter, *Nuclear Transplantation in Mouse Embryos*, 228 J. EXP. ZOOL. 355 (1983).

62. *See* MCKINNELL, *supra* note 47, at 88.

63. *See id*.

64. *See supra* Part II.B.

65. *See* K.H.S. Campbell et al., *Sheep Cloned by Nuclear Transfer from a Cultured Cell Line*, 380 NATURE 64 (1996).

66. *See* Wilmut, *supra* note 2, at 812.

67. *See id.* at 813.

"quiescence," meaning that the cells stopped dividing.[68] The scientists then removed the nucleus of an unfertilized egg drawn from a Scottish Blackface ewe and injected the quiescent nucleus from the mammary gland into the unfertilized egg.[69] The researchers used a pulse of electricity to activate the quiescent cell, and then implanted the egg into the reproductive chamber of a Blackface ewe.[70] This process was repeated 277 times until the experiments resulted in the birth of an apparently normal and healthy Finn Dorset lamb — Dolly.[71]

With the birth of Dolly, the Roslin researchers successfully demonstrated that a live mammal could be produced from a differentiated adult cell. While some questioned whether the cell used was really "differentiated" in the manner the experiment claimed,[72] the research generated great excitement because it seemed inescapably to suggest that the process of differentiation could be reversed, and that adult cells could be reprogrammed. This conclusion was certainly promising and opened up an area of research many had thought impossible. Nevertheless, it was necessary to duplicate the process before the real implications of the breakthrough could be assessed.[73]

More than a year after Dolly's birth, the journal *Nature* announced that a group of scientists at the University of Hawaii had succeeded in duplicating the Roslin Institute's technique with mice.[74] These researchers removed the nucleus from an egg cell and replaced it with the nucleus of a differentiated granulosa cell (a type of cell that surrounds the egg).[75] The result of this experiment was the production of twenty-two cloned mice, proving that the technique pioneered at the Roslin Institute was not an anomaly.[76] Furthermore, the successful nuclear transfer from adult cells in mice and the consequent extension of nuclear transfer technology is significant because mice, being easier

68. *See id*.
69. *See id*.
70. *See id*.
71. *See id*.
72. *See* Vittorio Sgaramella & Norton D. Zinder, *Counting Sheep — Dolly Confirmation*, 279 SCIENCE 635 (1998) (suggesting that Dolly might actually have been cloned through a fetal cell). The use of DNA testing laid these doubts to rest. *See* David Ashworth et al., *DNA Microsatellite Analysis of Dolly*, 394 NATURE 329 (1998) (using microsatellite analysis); Esther N. Signer et al., *DNA Fingerpriting Dolly*, 394 NATURE 329 (1998) (employing DNA "fingerprinting" techniques).
73. For an example of the skepticism with which some scientists regarded Dolly's arrival, see Sgaramella & Zinder, *supra* note 72 (noting that a single example of cloning from an adult cell could not be taken seriously until it was repeated).
74. *See* T. Wakayama et al., *Full-Term Development of Mice from Enucleated Oocytes Injected with Cumulus Cell Nuclei*, 394 NATURE 369 (1998).
75. *See id.* at 373.
76. *See* Davor Solter, *Dolly is a Clone — And No Longer Alone*, 394 NATURE 315, 315 (1998).

to work with than larger mammals, present greater opportunities for scientific research into the cloning of mammals.[77]

More recent developments confirm the rapid advances in cloning research and exacerbate fears that the specter of human clones looms in the near future. Scientists have succeeded in reducing the error rates in experiments involving large mammals, such as sheep and cows.[78] Furthermore, the recent production of a litter of cloned pigs has offered researchers renewed hope that these animals could be used as a source of organs for transplant into humans.[79] In addition, scientists have successfully used nuclear transfer technology in monkeys, an animal whose genetic similarity to humans heightens fears that a human clone will soon be a reality.[80] If scientists continue to overcome the technological difficulties, a legal regime that can address the possibility of human cloning may be the only means of controlling the use of this revolutionary technology.

The cloning of Dolly and other recent advances in cloning technology have fueled excitement in the scientific community because of the research possibilities they offer. However, they also have sparked controversy because of the moral and ethical implications of cloning a human being. Whatever their personal views, most researchers now regard the cloning of a human being as a matter of when, not if. It is this possibility that has generated efforts to design a regulatory approach that permits continued beneficial advances in genetic technology, while curbing efforts to create human beings. The FDA's assertion of regulatory jurisdiction so far represents the only authoritative step in this process.

III. THE FDA CLAIMS JURISDICTION

No "inside" account of the FDA's decision to assert jurisdiction over cloning has yet appeared. We may never know whether the Clinton White House pressured the Agency to act in order to forestall restrictive legislation or whether the Agency took the initiative despite administration reluctance. Nor has the FDA offered a full-blown defense of its legal reasoning, complete with consideration of

77. *See id*.

78. *See, e.g.*, Rick Weiss, *Clone Defects Point to Need for 2 Genetic Parents*, WASH. POST, May 10, 1999, at A1 (noting, however, that in large mammals, about half of all clones that develop into fetuses have serious abnormalities).

79. *See* Rick Weiss, *In Organ Quest, Cloning Pigs May Be the Easy Part*, WASH. POST, Mar. 20, 2000, at A7.

80. *See* Rick Weiss & John Schwartz, *Monkeys Cloned for First Time; Oregon Scientists Created Clones from Embryos Not Adult Cells*, WASH. POST, Mar. 2, 1997, at A4.

alternatives and explanation of its rejection of plausible objections, as it would have been obliged to do if it had thought it necessary to comply with the rulemaking requirements of the APA.[81] The Agency's explanation appears in a series of less formal statements that elaborate its reasoning but, even when read together, leave important questions unaddressed.

This Part begins by describing the FDA's steps to assert authority to regulate experimental efforts to clone a human being. It then examines the legal theory on which the Agency now seems to rely and discusses other potential legal theories that others urged upon it. Thereafter, this Part explores the practical implications of FDA regulation of biomedical researchers and their sponsors.

81. APA, 5 U.S.C. § 553 (2000).

A. The FDA's Public Explanation

On the heels of Dr. Seed's announcement, Congress was flooded with bills intended to prohibit his threatened service.[82] Several bills went even further, creating alarm that they would bar techniques holding promise to treat disease or advance agriculture.[83] In particular, representatives of the U.S. pharmaceutical industry became concerned that Congress might enact legislation stifling promising lines of medical research. They urged the Clinton White House to find an administrative means of preventing attempts to clone a human being, thereby obviating the need for legislation. In letters to the White House and HHS Secretary Shalala, the Pharmaceutical Research and Manufacturers of America ("PhRMA") and the Biotechnology Industry Organization ("BIO") argued that the FDA already possessed authority to forestall the kinds of experiments that excited public concern, such as Dr. Seed's, without jeopardizing important research.[84] BIO submitted a legal memorandum analyzing various statutory provisions that might give the FDA the authority to act.[85]

It is not clear whether the FDA welcomed this advice. The Agency's initial actions — a series of informal announcements spread over several months — suggest that it may have been reluctant to intrude into the contentious debate. The Agency's failure to conduct any formal proceedings to explore the meaning of existing laws or the options they afforded should surely prompt caution, if not reticence. In addressing a high-profile issue, the FDA has pursued a low-profile strategy.

The first signal that the FDA would seek to regulate cloning occurred during an interview on National Public Radio featuring the then-Acting FDA Commissioner, Dr. Michael Friedman. In response to a question, Dr. Friedman reportedly declared, "[t]hrough the Food, Drug, and Cosmetic Act we do have the authority to regulate human

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82. *See* Richard Saltus, *Are We Getting Closer to Cloning Humans*, BOSTON GLOBE, Sept. 5, 2000, at C1.

83. For a useful account of these efforts in Congress, see Elizabeth C. Price, *Does the FDA Have Authority to Regulate Human Cloning?*, 11 HARV. J.L. & TECH. 619, 625–26 (1998). *See also* Gregory J. Roskosz, *Human Cloning: Is the Reach of FDA Authority Too Far a Stretch?*, 30 SETON HALL L. REV. 464, 465 (2000); Valerie S. Rup, *Human Somatic Cell Nuclear Transfer Cloning, the Race to Regulate, and the Constitutionality of the Proposed Regulations*, 76 U. DET. MERCY L. REV. 1135, 1136–37 (1999).

84. *See* Letter from Carl B. Feldbaum, President, Biotechnology Industry Organization, to Donna E. Shalala, Secretary of Health and Human Services (Jan. 13, 1998) (published in FDA WEEK, Jan. 16, 1998, at 8); *Cloning Bill Frenzy Starts on Capitol Hill*, FDA WEEK, Feb. 6, 1998, at 16 (showing PhRMA support for FDA regulation in lieu of potentially overbroad federal or state legislation).

85. *See* Robert P. Brady & Molly S. Newberry, *FDA's Existing Statutory and Regulatory Authority Give the Agency the Broad Authority to Regulate the Cellular Materials Involved in Human Cloning*, FDA WEEK, Feb. 27, 1998, at 17.

cloning and we are prepared to assert that authority."[86] Dr. Friedman said that human cloning presented "serious health and safety issues" for both the fetus and mother.[87] He went on to say that the FDA viewed human cloning as another form of gene therapy, over which the Agency already exercised regulatory control.[88] Though appearing in print only in secondary accounts of the radio broadcast, Dr. Friedman's comments drew immediate attention.[89]

Several days later, the FDA's position was reaffirmed in a letter from the Agency's Deputy Commissioner for External Affairs, Sharon Smith Holston, to Senator Edward Kennedy, who was then sponsoring what was supposed to be narrow legislation banning any attempt to clone a human being. Possibly to persuade Kennedy that new legislation was not necessary, Ms. Holston wrote:

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86. Weiss, *supra* note 12, at A1; *see also FDA Has Authority to Regulate Cloning Technology As Biologic Product: Agency States After Chicago Physicist Seed Announces Plan for Human Cloning Clinic*, HEALTH NEWS DAILY, Jan. 13, 1998; *FDA Asserts Authority to Regulate Human Cloning: An Out for Industry Wary of Legislative Ban?*, THE PINK SHEET, Jan. 19, 1998.

87. *See* Weiss, *supra* note 12, at A1.

88. For a history of the FDA's role in overseeing gene therapy research, see Richard A. Merrill & Gail H. Javitt, *Gene Therapy, Law and FDA Role in Regulation*, in ENCYCLOPEDIA OF ETHICAL, LEGAL, AND POLICY ISSUES IN BIOTECHNOLOGY 321 (Thomas J. Murray & Maxwell J. Mehlman, eds., 2000) [hereinafter Merrill & Javitt]. There is a certain irony in Dr. Friedman's claim that human cloning is just another version of a medical technology that the FDA already regulated, given later reports of the failure of regulatory oversight by both the Agency and the National Institute of Health's Recombinant DNA Advisory Committee. *See* Wilder J. Leavitt, *Regulating Human Gene Therapy: Legislative Overreaction to Human Subject Protection Failures*, 53 ADMIN. L. REV. 315 (2001); FOOD AND DRUG ADMINISTRATION, PROPOSED APPROACH TO REGULATION OF CELLULAR AND TISSUE-BASED PRODUCTS 6 (1997), *at* http://www.dtincusa.com/June1/For%20June%201/Biologics/CELLTISSUE.pdf; DEPARTMENT OF HEALTH AND HUMAN SERVICES, OFFICE OF THE INSPECTOR GENERAL, FDA OVERSIGHT OF CLINICAL INVESTIGATORS (June 2000), *at* http://www.hhs.gov/oig/oei/reports/a457.pdf; DEPARTMENT OF HEALTH AND HUMAN SERVICES, OFFICE OF THE INSPECTOR GENERAL, RECRUITING HUMAN SUBJECTS: PRESSURES IN THE INDUSTRY-SPONSORED CLINICAL RESEARCH (June 2000), *at* http://www.hhs.gov/oig/oei/reports/a458.pdf; Abbey S. Meyers, *Gene Therapy: Balancing the Promise with the Reality*, THE EXCEPTIONAL PARENT, Mar. 1, 2000, at 20; Chris Adams, *Committee Pushes to Regain Authority over Experiments in Gene Therapy*, WALL ST. J., Nov. 26, 1999, at B6; Edward T. Pound, *Protections Found Lacking Follow-up Report: People in Medical Studies Still at Risk*, USA TODAY, Apr. 12, 2000, at A2 (discussing HHS Inspector General June Gibbs Brown's report on FDA and NIH oversight of clinical trials).

89. *See, e.g.*, Ted Bunker, *As Cloning Debate Heats Up, FDA Heads Off Congress*, BOSTON HERALD, Jan. 26, 1998, at 24; Arthur L. Caplan, *Why The Rush to Ban Cloning?*, N.Y. TIMES, Jan. 28, 1998, at A25; Caroline Daniel, *Human Cloning May Have Nothing on Earth to Stop It/Congress Has Failed to Pass Legislation That Could Block the Process*, HOUSTON CHRONICLE, Aug. 3, 1998, at 5A; Lisa Seachrist, *BIO Says Human Cloning Falls Under FDA's Purview*, BIOWORLD TODAY, Jan. 15, 1998, at 5A; Sheryl Gay Stolberg, *A Small Spark Ignites Debate on Laws on Cloning Humans*, N.Y. TIMES, Jan. 19, 1998, at A11.

> FDA already has jurisdiction over such experiments and is prepared to exercise that jurisdiction. While FDA's authority does not address the larger question of whether or not creating a human being using cloning technology should be altogether prohibited, this authority will ensure that such experimentation does not proceed until basic questions about safety are answered.[90]

The predictable *in terrorem* effect of these statements was almost certainly intended: Dr. Seed and possibly other researchers were forced to rethink their plans.[91] The FDA apparently wanted to discourage further experimentation by individual researchers, at least until the subject could be fully debated, though it did not offer to provide a forum for such debate. The Clinton Administration may have seen the FDA's claim of authority as a way of forestalling restrictive legislation,[92] but no administration or agency official attempted to describe the experiments required to be reviewed by the FDA or the standards to be applied in judging these experiments.

Several months passed before the FDA publically revisited the subject of cloning. Then, in October 1998, Dr. Stuart Nightingale, the FDA's Associate Commissioner for Medical Affairs, sent a letter to the nation's several hundred institutional review boards, setting forth the Agency's expectations. Dr. Nightingale's letter was the first extended explanation of the FDA's position and we therefore quote it at length:

> The purpose of this letter is to confirm to institutional review boards (IRBs) that the Food and Drug Administration (FDA) has jurisdiction over clinical research using cloning technology to create a human being, and to inform IRBs of the FDA regulatory process that is required before any investigator can proceed with such a clinical investigation. . . . As described more fully below, the appropriate mechanism to pursue a clinical investigation using cloning technology is the submission of an investigational new drug application (IND) to FDA.

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90. Letter from Sharon Smith Holston, Deputy Commissioner for External Affairs, FDA, to Senator Edward M. Kennedy (Feb. 10, 1998) (published in 144 CONG. REC. S561 (1998)).

91. *See* Weiss, *supra* note 12, at A1.

92. *See id.*; Sheryl Gay Stolberg, *FDA Stand On Cloning Raises Even More Questions*, N.Y. TIMES, Jan. 21, 1998, at A14; Bunker, *supra* note 89, at 24.

> Clinical research using cloning technology to create a human being is subject to FDA regulation under the Public Health Service Act and the Federal Food, Drug, and Cosmetic Act. Under these statutes and the FDA's implementing regulations, before such research may begin, the sponsor of the research is required to submit to the FDA an IND describing the proposed research plan; to obtain authorization from a properly constituted and functioning IRB; and to obtain a commitment from the investigators to obtain informed consent from all human subjects of the research. Such research may proceed only when an IND is in effect. Since the FDA believes that there are major unresolved safety questions pertaining to the use of cloning technology to create a human being, until those questions are appropriately addressed in the IND, the FDA would not permit any such investigation to proceed.
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> The FDA may prohibit a sponsor from conducting a study proposed in an IND application (often referred to as placing the study on "clinical hold") for a variety of reasons. If the Agency finds that "human subjects are or would be exposed to an unreasonable and significant risk of illness or injury," that would be sufficient reason to put a study on clinical hold. Other reasons listed in the regulations include "the IND does not contain sufficient information required . . . to address the risks to subjects of the proposed studies," or "the clinical investigators . . . are not qualified by reason of their scientific training and experience to conduct the investigation."[93]

Even as an ensemble, these FDA statements left crucial questions unanswered. None said, for example, what applications of cloning technology the FDA *believes* it has authority to regulate. Dr. Friedman's original statement that agency approval was required for any attempt to "clone a human being" suggested a limited focus.[94] Ms. Holston's letter referred more loosely to "human cloning experiments."[95] Dr. Nightingale's letter revived Dr. Friedman's formulation, "clinical research using cloning technology to create a human being."[96] His letter, though, did not indicate whether this concept will be interpreted

93. Nightingale Letter, *supra* note 15.
94. *See* Weiss, *supra* note 12, at A1.
95. *See* Holston, *supra* note 90.
96. Nightingale Letter, *supra* note 15.

to reach only experiments whose immediate goal is the creation of a human being or, more broadly, to encompass experiments whose results could advance understanding of how a human clone might be produced.

Dr. Nightingale's letter did clarify the formal means by which the FDA would exert authority, i.e., the Agency's process to oversee clinical studies of new medicines, known as the IND process. It emphasized the role of local IRBs, the entities that must approve clinical trials of investigational drugs or medical devices — a role with which most clinical researchers are undoubtedly familiar. Dr. Nightingale did not, however, offer IRBs much guidance on how they were to fulfill their central responsibility, the assessment of the "safety" of cloning experiments. Nor did he suggest whether IRBs should address other, arguably deeper, issues raised by proposed research protocols.

The FDA's assertion of jurisdiction over human cloning research may not have surprised informed observers of the Agency. The FDA had previously asserted authority to regulate other genetic technologies. For example, like conventional drugs manufactured by chemical synthesis, therapeutic agents produced through genetic engineering have traditionally been subject to premarket review for safety and effectiveness.[97] More relevantly, the FDA has exercised authority to approve and oversee gene therapy experiments on the theory that they involve the administration of "investigational drugs" to human subjects.[98] Dr. Friedman's description of human cloning experiments as a form of gene therapy thus not only had superficial plausibility, but, more importantly, it suggested that the FDA was already equipped to assess the research protocols that, by his account, required agency approval.

The FDA's invocation of its IND regime had the effect of imposing a moratorium on much domestic human cloning research.[99] The Agency's casual description of the kinds of experiments subject to its jurisdiction placed investigators and their sponsors at legal risk if they failed to seek and secure agency approval. Moreover, Dr. Nightingale's observation, that "major unresolved safety questions pertaining to the use of cloning technology" had to be resolved,[100] made clear that any research proposal would face rejection by the Agency even if it passed muster with a local IRB.

There is no evidence that any researcher sought FDA (or IRB, for that matter) approval for any cloning experiment following Dr. Nightingale's letter. Indeed, there have been no reports of any INDs

97. *See* PETER BARTON HUTT & RICHARD A. MERRILL, FOOD AND DRUG LAW: CASES AND MATERIALS 976 (2d ed. 1991) [hereinafter Hutt/Merrill Casebook].

98. *See* Merrill & Javitt, *supra* note 88, at 330.

99. *See* Weiss, *supra* note 12, at A1.

100. Nightingale Letter, *supra* note 15.

being submitted, much less approved, for such experiments through the present date. This is not to suggest, however, that no such experiments have been contemplated or undertaken. Indeed, earlier this spring, the FDA was inspired to reiterate its claim to regulatory jurisdiction, and in the process to elaborate its legal reasoning, in response to reports that a U.S. researcher and a compatriot in Italy were planning to produce the first human clone. On March 28, 2001, the Oversight and Investigations Subcommittee of the House Committee on Energy and Commerce convened a hearing to inquire into these reports and to learn about the government's plans to regulate cloning research. The Director of the FDA's Center for Biologics Evaluation and Research, Dr. Kathryn Zoon, was among the featured witnesses.[101]

In a brief prepared statement, Dr. Zoon described her Agency's concerns and outlined the regulatory requirements that, she asserted, existing law imposed:

> FDA views the use of cloning technology to clone a human being as a cause for public health concern. . . . Because of unresolved safety questions on the use of cloning technology to clone a human being, FDA would not permit the use of cloning technology to clone a human being at this time.
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> . . .
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> . . . My hope today is to clarify FDA's role in regulating the use of cloning technology to clone a human being and to discuss the significant scientific concerns regarding safety that would lead us at this time to disallow any such activities. It is important to note that FDA's role in assessing the use of cloning technology to clone a human being is a scientific one. As recognized by the National Bioethics Advisory Commission, there are additional unresolved issues

101. *See* Zoon Testimony, *supra* note 17, at 78. Other witnesses included Dr. Thomas B. Okarma (President and CEO, Geron Corporation), Dr. Rudolf Jaenishch (Professor of Biology, Massachusetts Institute of Technology), Dr. Brigitte Boisselie (Visiting Assistant Professor of Chemistry, CloneAid), Dr. Mark E. Westhusin (Associate Professor, Texas A&M University College of Veterinary Medicine), Dr. Panos Michael Zavos (Founder, Director, and Chief Andrologist, Andrology Institute of America), Dr. Thomas Murray (NBAC), Dr. Gregory Pence (Professor of Philosophy, University of Alabama at Birmingham), Mr. Randolphe H. Wicker (Founder, Clone Rights United Front), Dr. Arthur L. Caplan (Director, Center of Bioethics at the University of Pennsylvania), Sharon Terry (Genetics Alliance, Inc.), Dr. Nigel M. De S. Cameron (Principal, Strategic Futures Group, LLC), Dr. Michael Soules (President, American Society of Reproductive Medicine), Rael (Leader of the Raelian Movement), Mr. Jaydee Hanson (Assistant General Secretary, The United Methodist Church), and Mr. Mark Donald Eibert (Law Offices of Mark Eibert).

> including the broader social and ethical implications of the use of cloning technology to clone a human being. Because of the profound moral, ethical, and scientific issues, the Administration is unequivocally opposed to the cloning of human beings.[102]

With this preamble to her description of the FDA's plans, Dr. Zoon seemed to be sending a message. The last quoted sentence sets forth the predictable administration position on cloning generally and apparently draws a distinction between the "moral" and "ethical" concerns underpinning the administration's opposition and the Agency's own "scientific" concerns about safety. Dr. Zoon does not suggest, in this passage or later, that the FDA assumes any responsibility for addressing the "moral" or "ethical" issues. Thus, she raised the implication that resolution of the Agency's doubts about safety would fulfill its regulatory responsibilities. She later acknowledged this implication by responding in the negative when pointedly asked whether the FDA could or would attempt to prevent an experiment if the Agency were satisfied that it posed no health risk to the clone or its "mother."[103]

After stating the basis for the FDA's assertion of jurisdiction, Dr. Zoon's statement briefly described the evolution of somatic cell nuclear transfer, the technique used to clone Dolly. Finally, the statement turned to the FDA's legal rationale, which we quote in full:

> FDA has the authority to regulate medical products, including biological products, drugs, and devices. The use of cloning technology to clone a human being would be subject to both the biologics provisions of the Public Health Service (PHS) Act and the drug and device provisions of the Federal Food, Drug, and Cosmetic (FD&C) Act.
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> In response to questions about cellular products, in October 1993, FDA published a notice in the Federal Register, . . . clarifying the application of FDA's statutory authorities to human somatic cell therapy and gene therapy products. The notice stated that somatic cell therapy products are biological products under the PHS Act as well as drugs under the FD&C Act and are subject to investigational new drug (IND) application requirements. In the notice, FDA defined somatic cell therapy products as "autologous (i.e., self), allogeneic

102. *Id.* at 79–80.
103. *Id.* at 90.

> (i.e., intra-species), or xenogeneic (i.e., inter-species) cells that have been propagated, expanded, selected, pharmacologically treated, or otherwise altered in biological characteristics ex vivo to be administered to humans . . . ."
>
> Subsequently, in March 1997, the Agency proposed a more comprehensive regulatory approach for cellular and tissue-based products that includes somatic cell therapy products (62 FR 9721 March 4, 1997). In January 2001, after issuing and reviewing comments on a proposed rule, FDA issued a final rule that establishes the regulatory approach for human cells, tissue, cellular, and tissue-based products and requires establishments to register with the Agency and list their products.
>
> Clinical research using cloning technology to clone a human being is subject to FDA regulation under the PHS Act and the FD&C Act. Before such research could begin, the researcher must submit an IND request to FDA, which FDA would review to determine if such research could proceed. FDA believes that there are major unresolved safety questions on the use of cloning technology to clone a human being and therefore would not permit any such investigation to proceed at this time.[104]

Dr. Zoon then described the requirements of the FDA's IND regulations and the Agency's previous efforts to inform the research community of these requirements. In addition to Dr. Nightingale's 1998 letter described above, these efforts included an undescribed number of additional communications with "individuals or entities that expressed an intention to pursue the use of cloning technology to clone a human being."[105]

Dr. Zoon's prepared statement and her responses to questions constitute the FDA's most extended public description of the Agency's concerns about human cloning and the laws and regulations that, in the Agency's view, authorize it to regulate at least some cloning experiments. Yet, even when combined with its earlier brief statements, the Agency's account is unsatisfying. Repetition often serves as a substitute for explanation. Discontinuities and gaps in the historical record are overlooked, and legitimate and difficult questions about the Agency's interpretation of statutes are ignored. Perhaps most troubling

104. *Id.* at 80–81.
105. *Id.* at 81.

is the FDA's and the Administration's failure to explain how or whether to integrate an exploration of the profound ethical and moral issues raised by cloning with the inevitable efforts to address the more traditional questions about the procedure's safety.

The FDA's assertion of jurisdiction over cloning has not been judicially challenged, and there is no evidence that such a challenge is likely soon. An immediate legal challenge to the FDA's jurisdiction could face procedural obstacles.[106] It is, therefore, conceivable that the FDA's implicit assertion that Congress need not enact new legislation to regulate efforts to clone a human being will become "law" without further debate. In our view, this would be unfortunate. The legal bases of the FDA's action and, just as important, its capacity to address the full range of issues involved in human cloning research deserve a more thorough analysis. Before proceeding with this analysis, however, we examine the FDA's customary role in the regulation of medical research, the role that the Agency claims entitles it to regulate cloning experiments.

B. The FDA's Oversight of Clinical Research

No agency of the *federal* government has plenary jurisdiction over all medical research involving human subjects. Federal oversight of such experiments is widespread, however, because the two circumstances in which this oversight *is* authorized by statute comprise the bulk of the medical clinical research conducted in this country.

The FDA's parent, the Department of Health and Human Services, has jurisdiction over human research supported by HHS funds or conducted at institutions receiving HHS funds.[107] A second body of clinical research subject to federal regulation are experiments sponsored by companies requiring FDA approval to market new medical products.[108] This second (and overlapping) category encompasses a

106. Since the FDA has not purported to issue any new regulations, a plaintiff could not rely on the FDCA provision permitting preenforcement review of rules implementing the FDCA's IND authority. *See* 21 U.S.C. §§ 355(i), 371(f)–(g) (2000). Furthermore, a court might well dismiss as premature a suit challenging the FDA's claim that its IND regulations apply to cloning experiment. *See* AMP, Inc. v. Gardner, 389 F.2d 825 (2d Cir. 1968), *cert. denied*, 393 U.S. 825 (1968). *But see* Appalachian Power Co. v. EPA, 208 F.3d 1015 (D.C. Cir. 2000).

107. *See* HHS FACT SHEET: PROTECTING RESEARCH SUBJECTS, *available at* http://www.hhs.gov/news/press/2000pres/20000606a.html (last modified June 6, 2000).

108. *See, e.g.*, Hutt/Merrill Casebook, *supra* note 97, at 21; Richard A. Merrill, *Symposium on Regulating Medical Innovation: The Architecture of Government Regulation of Medical Products*, 82 VA. L. REV. 1753, 1753 (1996). Not all clinical studies of drugs and devices are sponsored by manufacturers or conducted for the purpose of gaining FDA approval for marketing. Many are sponsored by NIH and thus are subject to federal oversight on that ground alone, and others are undertaken by individual

major part of the clinical research conducted in U.S. medical centers and other health care institutions.[109] FDA oversight is thus an important feature of the medical research environment in this country. The Agency's jurisdiction is not unlimited, however. Its authority depends on the purpose for which research is undertaken and, just as importantly, on the substances or products to which research subjects are exposed.[110] Stated simply, the FDA only has the authority to regulate human research involving "articles" — the statutory term — whose commercial distribution the Agency can regulate.[111]

This universe consists mainly of products marketed to improve human health[112] and is comprised of three statutory categories: drugs, medical devices, and biological products.[113] The FDA's authority over

investigators who obtain IND approval to study possible beneficial effects of agents approved for other indications, agents they cannot otherwise lawfully obtain. The majority of such studies, however, are manufacturer-sponsored and are undertaken to obtain evidence to support applications for marketing approval.

109. *See, e.g.*, Merrill, *supra* note 108, at 1775.

110. *See* 21 U.S.C. § 321(g)(1) (2000).

111. *See id*.

112. The FDA also regulates food and cosmetics and certain radiation-emitting products, like microwave ovens. Development of these products rarely involves testing on human subjects. *See* Hutt/Merrill Casebook, *supra* note 97, at 23–37, 794–806, and 814–62. This part focuses on the FDA's authority to regulate products to which human beings are commonly exposed in experimental settings and its derivative authority to regulate such experiments.

113. "The term 'drug' means (A) articles recognized in the official United States Pharmacopoeia, official Homeopathic Pharmacopoeia of the United States, or official National Formulatory, or any supplement to any of them; and (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and (D) articles intended for use as a component of any article specified in clause (A), (B), or (C) of this paragraph. A food or dietary supplement for which a claim, subject to sections 343(r)(1)(B) and 343(r)(3) of this title or sections 343(r)(1)(B) and 343(r)(5)(D) of this title, is made in accordance with the requirements of section 343(r) of this title is not a drug solely because the label or the labeling contains such a claim. A food, dietary ingredient, or dietary supplement for which a truthful and not misleading statement is made in accordance with section 343(r)(6) of this title is not a drug under clause (C) solely because the label or the labeling contains such a statement." FDCA, 21 U.S.C. § 321(g)(1)(2000).

"The term 'device' (except when used in paragraph (n) of this section and in sections 331(i), 343(f), 352(c), and 362(c) of this title) means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is (1) recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them, (2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or (3) intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purpose." FDCA, 21 U.S.C. § 321(h) (2000).

drugs and medical devices comes from the FDCA.[114] Its authority over biological products stems from Section 351 of the laws that are now collectively codified as the Public Health Service Act.[115] The FDA must approve virtually all new human drugs and new life-sustaining and implantable medical devices before they may be marketed.[116] Biological products, such as vaccines, similarly require FDA licensing before they may be distributed.[117] It is the FDA's power to regulate the marketing of such products — technically, their distribution in interstate commerce — that is the source of its legal authority over clinical research. Although derivative, this authority is far-reaching.

To simplify presentation, this discussion focuses on the FDCA's requirements for so-called "new drugs."[118] It is these requirements on

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"The term 'biological product' means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings." PHSA, 42 U.S.C. § 262(i) (2000).

114. FDCA, 21 U.S.C. §§ 301–397 (2000).

115. PHSA, 42 U.S.C. §§ 201–300 (2000).

116. *See* Hutt/Merrill Casebook, *supra* note 97, at 752.

117. *See id.* at 663–64.

118. "The term 'new drug' means — (1) Any drug (except a new animal drug or an animal feed bearing or containing a new animal drug) the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof, except that such a drug not so recognized shall not be deemed to be a 'new drug' if at any time prior to the enactment of this Act [enacted June 25, 1938], it was subject to the Food and Drugs Act of June 30, 1906, as amended, and if at such time its labeling contained the same representations concerning the conditions of its use; or (2) Any drug (except a new animal drug or an animal feed bearing or containing a new animal drug) the composition of which is such that such drug, as a result of investigations to determine its safety and effectiveness for use under such conditions, has become so recognized, but which has not, otherwise than in such investigations, been used to a material extent or for a material time under such conditions." FDCA, 21 U.S.C. § 321(p) (2000). This complicated definition, made part of the FDCA in 1962, was intended to exclude from the FDA's premarket approval requirements those drugs marketed prior to the 1938 Act for which physician or patient experience provided confirmation of safety and, later, effectiveness. While a few so-called "old" prescription medicines remain in use (e.g., digitalis), the vast majority of prescription drugs marketed in the U.S. have gone through the FDA's new drug approval process. Additionally, novel medical agents indisputably must satisfy the Agency's requirements.

This simplification does not undermine the fundamental accuracy of the preceding description. Although the PHSA does not expressly authorize the FDA to regulate pre-marketing research on biological products, the Agency has appropriately held that biologicals are also "drugs" and therefore subject, prior to marketing, to the FDCA's requirements for "investigational new drugs." Unlike drugs and biologicals, not all medical devices require premarket approval for safety and effectiveness, but a significant number, consisting of the highest-risk devices, do, and the FDCA authorizes the FDA to oversee clinical research involving such devices. The oversight regime for

which the FDA ultimately relies to support its jurisdiction over cloning experiments. Since 1962, the FDCA has required affirmative FDA approval for the marketing of any new drug.[119] The FDCA has also specifies that before granting approval, the Agency must be satisfied that the drug is both safe and effective for the use(s) that the manufacturer intends to promote in labeling and advertising.[120] To obtain sufficient evidence of safety and effectiveness, the manufacturer must conduct or sponsor trials in human subjects, most of whom will be patients suffering from the condition that the drug might treat.[121]

Almost always, the still-experimental drug must be shipped to the investigators who have agreed to conduct the clinical trials. Yet, in the absence of FDA marketing approval, such shipment would violate the law. To avoid this "Catch-22," Congress authorized the FDA to grant exemptions for drugs shipped solely for "investigational use," that is, for use in studies that will become part of an application for marketing approval.[122] The statute also directs the FDA to impose conditions that the manufacturer must satisfy to qualify for exemption — primarily conditions designed to protect the trial subjects' safety and autonomy.[123] Herein lies the source of the FDA's possible authority to regulate medical experiments involving human subjects including *some*, but certainly not *all*, "human cloning experiments."

Dr. Nightingale's letter and Dr. Zoon's recent testimony leave no doubt that, in asserting jurisdiction over cloning experiments, the FDA is relying on its authority to regulate clinical studies of unapproved new drugs. As the Supreme Court's rejection of the FDA's attempt to regulate tobacco illustrates,[124] however, the fact that the FDA claims authority is no guarantee that Congress has conferred it.

C. Other Legal Options

Before analyzing the legal theory on which the FDA does rely, this Part examines other theories that were presented to the Agency for consideration. Our framework is provided by the thoughtful memorandum submitted to the Clinton Administration on behalf of

"investigational devices" is similar to that for new drugs. *See* Human Drugs Which are Biological Products, 37 Fed. Reg. 4,004–05 (Feb. 25, 1972).

119. *See* Merrill, *supra* note 108, at 1765.

120. *See id*. at 1775.

121. *See* Michael D. Greenberg, Ph.D, *AIDS, Experimental Drug Approval, and the FDA New Drug Screening Process*, 3 N.Y.U. J. OF LEGIS. & PUB. POL'Y 295, 303–07 (2000).

122. *See* Merrill, *supra* note 108, at 1777.

123. *See* FDCA, 21 U.S.C. § 355 (2000).

124. *See* FDA v. Brown & Williamson Tobacco Corp., 529 U.S. 120 (2000).

BIO,[125] though we have seen no account of the FDA's own analysis of BIO's suggested options.

1. Option 1: Section 361 of the Public Health Service Act

The FDA was urged to consider Section 361 of the PHSA as a basis for exercising jurisdiction over human cloning experiments.[126] This provision, enacted a century ago, accords the Surgeon General (and, by delegation, the FDA) stunningly broad, albeit contextually confined, authority. In relevant part section 361(a) provides:

> The Surgeon General, with the approval of the Secretary, is authorized to make and enforce such regulations as in his judgment are necessary to prevent the introduction, transmission, or spread of communicable diseases from foreign countries into the States or possessions, or from one State or possession into any other State or possession. For purposes of carrying out and enforcing such regulations, the Surgeon General may provide for such inspection, fumigation, disinfection, sanitation, pest extermination, destruction of animals or articles found to be so infected or contaminated as to be sources of dangerous infection to human beings, and other measures, as in his judgment may be necessary.[127]

A companion provision, Section 368(a) of the PHSA, criminalizes violations of regulations issued pursuant to this grant of authority.[128]

BIO suggested that the FDA could use Section 361 to regulate human cloning based on the risk of transmission of HIV and other infectious diseases from the donor(s) of cellular material to a clone or its "mother."[129] Because the FDA had previously cited the risk of disease transmission as the justification for regulating the recovery and processing of transplantable human tissue (e.g., bone, skin, tendons), the suggestion was not implausible.[130]

There are, however, two difficulties with this suggestion that may explain the FDA's decision not to rely upon it. First, while the *measures*

125. *See* Brady & Newberry, *supra* note 85.
126. PHSA § 361, 42 U.S.C. § 264 (2000).
127. PHSA § 361, 42 U.S.C. § 264(a) (2000).
128. *See* PHSA § 368(a), 42 U.S.C. § 271(a) (2000).
129. *See* Brady & Newberry, *supra* note 85, at 17.
130. *See* Human Tissue Intended for Transplantation, 58 Fed. Reg. 65,514 (Dec. 14, 1993) (codified at 21 C.F.R. § 1270) [hereinafter Tissue for Transplantation].

authorized by Section 361 are described in broad terms, the ends at which such measures must be aimed are not. The only goal that Congress has authorized the Agency to pursue is prevention of communicable disease — a much narrower target than the manifold concerns about human cloning. Moreover, the FDA could have invoked Section 361 only if it had been prepared to initiate rulemaking, which would have required compliance with the APA.[131] The section has no operative force in the absence of regulations. The FDA's regulations governing transplantable human tissues are based on Section 361,[132] but their requirements, as we later explain, do not require processors or medical researchers to notify the Agency of, much less gain its approval for, any clinical use of tissue.

The FDA's failure to conduct *any* public proceeding to substantiate its assertion of jurisdiction over human cloning experiments suggests that it probably rejected the Section 361 option early in its planning. It may not only have been the prospect of having to explain its position that led the Agency to consider other options. The need for rulemaking to impose any restrictions on cloning experiments would have delayed regulation and thus undermined any administration claim of existing legal authority.

2. Option 2: The FDA's Human Tissue "Plan"

A second option proposed to the FDA was to rely on what has been called the FDA "plan for cellular and tissue-based products."[133] In 1997, the FDA released this document for public comment, but it has never formally proposed it as a rule. Its language would appear to contemplate the kind of restrictions on clinical research that the FDA later said apply to human cloning experiments. In order to explain why this option would not have accomplished the Agency's objectives, we must first recount the FDA's attempts to control the health hazards associated with tissue transplants.

Within the last generation, surgeons have come to use tissues harvested from cadavers in a wide range of medical procedures. Bone transplants are common in orthopedic surgery.[134] Oral surgeons use

131. *See* PHSA § 361, 42 U.S.C. § 264 (2000); APA, 5 U.S.C. § 553 (2000).

132. *See* 21 C.F.R. § 1270 (1999).

133. FOOD AND DRUG ADMINISTRATION, A PROPOSED APPROACH TO THE REGULATION OF CELLULAR AND TISSUE-BASED PRODUCTS, Feb. 28, 1997, *at* http://hayato.med.osakau.ac.jp/index/societies-j/tissue/fda970228_c.html [hereinafter FDA Plan].

134. *See* OFFICE OF THE INSPECTOR GENERAL, DEPARTMENT OF HEALTH AND HUMAN SERVICES, OVERSIGHT OF TISSUE BANKING 1 (Jan. 2001) [hereinafter TISSUE BANKING]; *see also* FDA Plan, *supra* note 133; *Tissue Banks: Is the Federal Government's Oversight Adequate?: Hearing Before the Permanent Subcomm. on Investigations of the Senate*

pulverized, demineralized cadaveric bone in many dental procedures.[135] Tendons, ligaments, skin, corneas, and dura matter (the outer covering of the brain) are other now-common surgical implants.[136] Until the 1980s, with isolated exceptions,[137] the FDA was either oblivious to or unconcerned about these surgical uses of processed human tissue. Officials may have viewed such procedures as part of the "practice of medicine," which the Agency has historically refrained from regulating.[138] But two developments — the emergence of AIDS and the technological advances within the "tissue industry" — galvanized the FDA into action nearly a decade ago.

It became clear in 1986 that HIV contamination of transplantable human tissue was more than a hypothetical possibility when a single infected donor was discovered to be the source of tissues implanted in more than two dozen patients — several of whom later became HIV positive.[139] The donor had been tested for HIV, but it later became evident that, although already infected, he had not developed detectable antibodies before he died. In December 1993, the FDA issued regulations mandating new procedures for tissue banks, which it made immediately effective after invoking the "good cause" exception to the APA's rulemaking requirements.[140] The Agency had not previously held that tissue banks or their products were within its jurisdiction.

Comm. on Governmental Affairs, 107th Cong. 3–4 (2001) (statement by Dr. Kathryn C. Zoon, Director for Biologics and Research, Food and Drug Administration), *available at* http://www.senate.gov/~gov_affairs/052401_zoon.pdf; Suitability Determination for Donors of Human Cellular and Tissue-Based Products, 64 Fed. Reg. 52,697 (proposed Sept. 30, 1999) (to be codified at 21 C.F.R. pts. 210, 211, 820, and 1271); FOOD AND DRUG ADMIN., DEP'T OF HEALTH AND HUMAN SERVS., *Tissue Action Plan: Reinventing the Regulation of Human Tissue*, NAT'L PERFORMANCE REV. (1997), *available at* http://www.fda.gov/cber/tissue/rego.htm.

135. *See* TISSUE BANKING, *supra* note 134.

136. *See id*.

137. *See* John Henkel, *Safeguarding Human Tissue Transplants*, FDA CONSUMER, Sept. 1, 1994, at 9, 10.

138. 21 U.S.C. § 396 (1997); *see also* Hutt/Merrill Casebook, *supra* note 97, at 621 (referencing Peter B. Hutt, *Regulation of the Practice of Medicine under the Pure Food and Drug Laws*, 33 Q. BULL. ASS'N FOOD & DRUG OFF. 1 (1969)); Edward M. Basile et al., *Medical Device Labeling and Advertising: An Overview*, 54 FOOD DRUG COSM. L.J. 519, 524 (1999).

139. *See* TISSUE BANKING, *supra* note 134, at 1.

140. Tissue for Transplantation, *supra* note 130. The FDA relied on the language in the APA, which permits an agency to dispense with prior notice and opportunity for comment when it "for good cause finds . . . that notice and public procedure . . . are impracticable, unnecessary, or contrary to the public interest." 5 U.S.C. § 553(b) (2000). The Agency contended that immediate imposition of requirements for the screening of donors, processing of tissue, and record requirements that would facilitate tracking of transplants was a matter of urgency. *See* Tissue for Transplantation, *supra* note 130, at 65,514.

In promulgating its new regulations, the FDA refrained from declaring that human tissues intended for transplantation were drugs, biological products, or medical devices, though it conceivably could have done so.[141] Instead, it relied exclusively on PHSA Section 361,[142] requiring banks to screen all tissue donors for disease, test all recovered tissue, and maintain processing and shipment records that would allow them to retrace any tissue later found to be from an infected source.[143] A final version of the FDA's tissue regulations was published in 1997. The final regulations establish the minimum federal requirements for the recovery, processing, and distribution of transplantable human tissues.[144] However, they do not impose any restrictions on the clinical *use* of appropriately screened and tested tissue. Nor do they require tissue banks to demonstrate that their products are safe or effective. Thus, the FDA could not have required advance approval of clinical human cloning experiments using cellular material even if it had defined that material as "human tissue."[145] To reach that goal, relying only on Section 361, the FDA would have had to amend its regulations.[146]

The 1997 regulations proved to be just one step in the FDA's ongoing effort to fashion a comprehensive regime for regulating the use of human materials. Objects of potential regulation include umbilical cord blood that is recovered at birth and stored for later therapeutic

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141. A decade earlier, in the context of congressional consideration of new federal legislation governing the recovery and allocation of transplantable organs, FDA had provided for the public record an equivocal analysis of its own potential jurisdiction under the laws for which it was then (and is still) responsible, the FDCA and the PHSA. Although this analysis did not unequivocally affirm the Agency's authority to regulate human organs as drugs, medical devices, or biological products, it explored each possibility in terms that suggest it could have justified regulation on any of these theories. *See Hearing Before the Subcomm. on Investigations and Oversight of the House Comm. on Sci. and Tech.*, 98th Cong., 1st Sess. (1983) (statement by FDA concerning its legal authority to regulate human organ transplants and to prohibit their sale), *reprinted in* Hutt/Merrill Casebook, *supra* note 97, at 693–94. Curiously, the subcommittee's printed report did not contain the FDA's statement.

142. Tissue for Transplantation, *supra* note 130, at 65,516.

143. *Id.* at 65,517–18.

144. *See id.*

145. Human tissue is defined as:

> any tissue derived from a human body, which: (1) Is intended for transplantation to another human for the diagnosis, cure, mitigation, treatment, or prevention of any condition or disease; (2) Is recovered, processed, stored, or distributed by methods that do not change tissue function or characteristics; (3) Is not currently regulated as a human drug, biological product, or medical device; (4) Excludes kidney, liver, heart, lung, pancreas, or any other vascularized human organ; and (5) Excludes semen or other reproductive tissue, human milk, and bone marrow.

21 C.F.R. § 1270.3 (2001).

146. *See* 21 U.S.C. § 355 (1999).

use[147] and cells extracted from a patient, processed outside the body to stimulate growth, and then reinjected to aid recovery from injury.[148] Although the FDA's actions might have been upheld if it had declared all such materials to be biological products or medical devices, it would not have been comfortable with either categorization. Declaring an article a biological product inexorably subjects it to the law's requirements for pre-marketing proof of safety and effectiveness, as well as the IND requirements for clinical studies of unapproved drugs.[149] Declaring tissue implant to be a device would invite classification in Class III, for which the FDCA similarly requires pre-marketing proof of safety and effectiveness — proof that can only be obtained through clinical experiments subject to the FDA's investigational device requirements.[150]

One can imagine several reasons why FDA officials have been reluctant to insist upon pre-market approval of all tissue-based therapies. To regulate all tissue transplants as biologics would bring the FDA close to regulating the practice of surgery. Furthermore, many transplant procedures have gained such wide acceptance that now demanding formal proof of safety and effectiveness would invite resistance. Finally, and perhaps most importantly, such a decision would dramatically increase the Agency's workload at a time when its resources are constrained.

At the same time, FDA officials were obviously uncomfortable with the status quo, in which novel tissue forms and uses were subject only to the donor screening and disease testing requirements of its 1997 regulations.[151] The "plan" for cellular and tissue-based products that the Agency released for public comment represents a first step toward resolving the dilemma.[152] This document describes a strategy for

147. *See* Request for Proposed Standards for Unrelated Allogeneic Peripheral and Placental/Umbilical Cord Blood Hematopoietic Stem/Progenitor Cell Products, 63 Fed. Reg. 2985 (Jan. 20, 1998).

148. *See* Letter from Jay P. Siegel, Director, Office of Therapeutics Research and Review, Center for Biologics Evaluation and Research, and Jerome A. Donlon, Director, Office of Establishment Licensing and Product Surveillance, Center for Biologics Evaluation and Research, to Tim Surgenor, Genzyme Corporation (August 22, 1997), *available at* http://www.fda.gov/cber/approvltr/autogen082297L.htm (authorizing the manufacture and sale of "autologous cultured chondrocytes" under the brand name Carticel).

149. A human drug product is "the active ingredient of a new drug or human biologic product" as those terms are used in the FDCA and the PHSA. 21 C.F.R. § 60.3 (2000).

150. *See* 21 U.S.C. § 360(c) (2000). For a discussion of the FDA's clinical testing of devices, see Merrill, *supra* note 108, at 1800–35.

151. The FDA had only declared a small number of tissue-based products to be devices and had opted instead to establish a general regulatory strategy that could guide future decisions.

152. *See* FDA Plan, *supra* note 133.

calibrating regulatory requirements to the risks of adverse reaction or product failure that a technology presents. For technologies posing low risks, compliance with the new regulations and other still-to-be-developed "good tissue practice" requirements — such as registration, product listing, and additional disease screening and testing — should suffice.[153] But the FDA plan also contemplates that cellular technologies may warrant more stringent controls, including mandatory clinical studies to demonstrate safety and effectiveness — a requirement triggered by an Agency determination that the implanted material is a biological drug.[154]

With this background, it is possible to imagine how the FDA plan might apply to human cloning. The plan indicates that the novelty of a procedure — measured by the extent to which human-source material is modified or put to an unfamiliar use — will guide the Agency's decision about what regulatory requirements should be imposed. But it was already clear that the FDA would likely consider some applications of cloning subject to regulation as biological drugs. The Agency's "plan" may have predicted how it might view cloning but it did not, and does not, provide independent authority for the restrictions the Agency seeks to impose.

First, the FDA's tissue plan has no legal force. Although the Agency did invite public comments and has often described the plan as "proposed," it has never published the plan in the Federal Register as a proposed, much less final, rule.[155] The plan embodies the Agency's thinking about how it should regulate technologies that use human tissue, including cellular material, but it does not legally bind either the Agency or the public.

Second, even if the FDA's plan had been promulgated as a regulation, it would not purport to require pre-marketing approval or clinical study of any specific technology. The document discusses the criteria the FDA will consider in deciding whether those requirements should apply to a technology. However, it leaves largely unexplained —

153. *See id.* at 11.

154. *See id.* at 12. The FDA recognizes that a triage strategy of the kind it has outlined requires criteria for distinguishing between low-risk technologies and technologies that warrant more stringent oversight. To make such distinctions, the Agency intends to focus on two questions. First, does the technology involve more than "minimal manipulation" of human material? Second, is the material, however prepared, intended for a "homologous use," i.e., a use similar to the function it served in the donor? If the answer to the first question is "yes," *or* the answer to the second is "no," the technology is a candidate for regulation as a biological drug or, possibly, as a medical device. *See id.* at 13–15.

155. The FDA did announce the availability of the plan by notice in the Federal Register. Proposed Approach to Regulation of Cellular and Tissue-Based Products, 62 Fed. Reg. 9721 (Mar. 4, 1997).

and so far ungoverned — the process by which such decisions will be made.[156] Furthermore, the plan does not identify any source of statutory authority, other than the FDCA and the Biologics Act, to impose such controls. In sum, the FDA's tissue plan is merely a forecast of the circumstances in which the Agency will resort to the FDCA's pre-market approval and IND requirements to regulate yet-to-be-designated therapeutic technologies.[157]

The Agency's past regulation of tissue reveals a gap that makes its eagerness to regulate human cloning mildly puzzling. Among the many medical uses of human tissue, transplantation of donated sperm, eggs, and, more recently, complete embryos to facilitate reproduction may be the most familiar. Such "reproductive tissues" can also be potential vectors for the transmission of donor disease. Yet, until very recently, the FDA had taken no steps to regulate purveyors of such tissues or to oversee the means by which they are recovered or the procedures in which they are used.[158] Indeed, the Agency expressly excluded reproductive tissues from its 1997 conventional tissue regulations.[159]

This omission was no oversight. The FDA's explicit declaration that its regulations would not apply to reproductive tissues confirms that agency officials were aware of their increasing use. Nor could the Agency have entertained serious doubts about its legal authority to regulate such tissues. If a cadaver heart valve may be regulated as a medical device, as the Agency had earlier claimed,[160] it would be no

156. This is perhaps something of an overstatement. The FDA has announced the establishment of an internal "Tissue Reference Group" ("TRG") consisting of officials from its Center for Biologics Evaluation and Research and its Center for Devices and Radiological Health, which is responsible for determining — so far as the Agency has authority to determine — how particular technologies should be regulated. *See* FDA Plan, *supra* note 133, at 13. Although the Agency has invited formal requests for determination from developers of technologies, the process by which the TRG will arrive at and communicate its determinations remains ill-defined and ad hoc. No provision has been made for inviting, or allowing for, comments from third parties including physicians, patients, professional associations, or other developers of technology.

157. The plan implies that before imposing on a particular cellular or tissue technology more rigorous standards than the basic requirements for "conventional" tissues, the FDA will announce its reasons and allow developers, users, and members of the public an opportunity to offer supporting or contradictory evidence and argument. *See id.* at 22–24.

158. In 1998, the Agency indicated in a proposed rule that, at some time in the near future, it would apply its general human tissue requirements to entities engaged in the recovery and transplantation of reproductive tissue. *See* Establishment Registration and Listing for Manufacturers of Human Cellular and Tissue-Based Products, 63 Fed. Reg. 26,744 (proposed May 14, 1998) (codified at 21 C.F.R. § 1271.3(d)(2) (effective Jan. 21, 2003)).

159. *See* Human Tissue Intended for Transplantation, 62 Fed. Reg. 40,429 (July 29, 1997); 21 C.F.R. § 1270.3 (2001).

160. *See* Alabama Tissue Ctr. of the Univ. of Alabama Health Serv. Found. v. Sullivan, 975 F.2d 373 (7th Cir. 1992).

greater stretch to claim that transplants of sperm, eggs, and oocytes are biological products. While we do not pause to speculate why the FDA long refrained from asserting jurisdiction over reproductive tissues,[161] this history does heighten curiosity about the Agency's eagerness to assert jurisdiction over human cloning — another form of "assisted reproduction."

3. Option 3: The FDA's Regulation of Gene Therapy

In his radio interview, Acting FDA Commissioner Friedman likened human cloning to gene therapy, which the FDA has regulated for several years.[162] In her recent congressional testimony, Center for Biologics Evaluation and Research ("CBER") Director Zoon quoted from the 1993 Federal Register notice, in which the FDA announced that it considered somatic cell therapy products to be both biological products and drugs.[163] In short, both contended that the statutory authority on which the Agency relies to regulate gene therapy also supports its jurisdiction over cloning experiments. Although this claim does not fully resolve the question of the FDA's authority, it does narrow the focus of our present inquiry and invite examination of the Agency's role in overseeing gene therapy research.

For the last decade the FDA has insisted that research protocols involving the insertion of somatic cells into human subjects must first be approved by the agency.[164] Its explicit legal premise is that such experiments involve the administration of investigational drugs, in the form of implanted material, and are therefore subject to FDCA Section 505(i).[165] The FDA's gene therapy research program is administered by Dr. Zoon's CBER, which purports to review protocols under the same standards that it applies in judging other clinical applications of biotechnology — but with an important variation.[166]

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161. It is possible, perhaps even likely, that the FDA was reluctant to acknowledge its authority to regulate a set of procedures that have excited intense interest, considerable controversy, and wide publicity. Proliferation of assisted reproduction services raises a set of questions almost as diverse and profound as those posed by human cloning. Furthermore, if the Agency were to enter the arena, it would surely face pressure from opponents of many of these services to go much further than "mere" public health concerns might lead it to go. Finally, in any setting, the FDA might confront real difficulty in establishing that the tissue in question had moved, or might move, in interstate commerce.

162. *See* Weiss, *supra* note 12, at A1.

163. *See* Zoon Testimony, *supra* note 17, at 80 (quoting 58 Fed. Reg. 53,248 (Oct. 14, 1993)).

164. *See* Merrill & Javitt, *supra* note 88, at 325–28.

165. *See* Establishment Registration and Listing for Manufacturers of Human Cellular and Tissue-Based Products, 63 Fed. Reg. 26,744 (May 14, 1998).

166. *See* Merrill & Javitt, *supra* note 88, at 322.

The novel element is a product of the original federal regime for overseeing recombinant DNA ("RDNA") technology. That regime reposed primary responsibility in the Recombinant DNA Advisory Committee ("RAC"), an entity established by the National Institutes of Health in 1974.[167] The RAC's formal jurisdiction was limited to experiments conducted or funded by federal agencies, but most private developers of RDNA technology voluntarily agreed to adhere to the RAC's guidelines. Accordingly, many privately-sponsored experiments have also been submitted for RAC review.[168] When pioneers in RDNA technology became interested in possible therapeutic applications and designed experiments in which foreign genes would be administered to human patients, the RAC shifted its focus. Risk to research subjects has commanded its attention in recent years.[169]

In 1991, the FDA advanced its own claim of authority to oversee gene therapy experiments[170] and for several years the RAC and the FDA competed to review gene therapy research protocols.[171] Over time, however, the two agencies reached an understanding.[172] The RAC concentrated on the ethical issues raised by proposed experiments, while the FDA focused on familiar FDCA issues — the immediate risk to patients, the potential for therapeutic benefit, and the reliability of the investigator's processes for preparing and administering the genetic material to be studied.[173]

By the late 1990s, the FDA had assumed the lead role in this partnership. The Agency reviewed all clinical applications of gene therapy, just as it had always reviewed clinical trials of conventional therapies, and NIH leaders even considered ending parallel RAC review.[174] This initiative was aborted, however, in part because the RAC's expertise was needed to evaluate the non-medical issues raised by

167. *See id.* The RAC's original focus was on experiments that could result in the release of genetically altered organisms into the environment.

168. *See id*.

169. *See id*.; *see also* Chris Adams, *Committee Pushes to Regain Authority over Experiments in Gene Therapy*, WALL ST. J., Nov. 26, 1999, at B6 (discussing the role of the FDA and the RAC in gene therapy and calling for expansion of the RAC's oversight); Abbey S. Meyers, *Gene Therapy: Balancing the Promise with the Reality*, EXCEPTIONAL PARENT, Mar. 1, 2000, at 20–24; *NIH's In-Depth Reply to Rep. Waxman on Gene Therapy Oversight*, BLUE SHEET, Apr. 12, 2000, at 12 (containing an Apr. 5, 2000 letter from NIH Acting Director Ruth Kirchstein to Rep. Henry Waxman in response to his Feb. 23, 2000 letter critiquing the Agency's oversight of gene therapy protocols).

170. *See* 21 U.S.C. § 355(a) (1999); Merrill & Javitt, *supra* note 88, at 324–25.

171. *See* Merrill & Javitt, *supra* note 88, at 324–27.

172. *See id.* at 322.

173. *See id.* at 328–29.

174. *See id*.

some protocols. Accordingly, the NIH, with FDA concurrence, preserved the RAC as the forum for their discussion.[175]

The FDA's regulation of gene therapy experiments may offer a precedent for its assertion of jurisdiction over cloning research, but it does not provide an independent legal basis for the position announced by Dr. Friedman and elaborated by Dr. Zoon. The FDA's regulation of gene therapy experiments is not based on an explicit legislative grant of jurisdiction. Rather, it is predicated on the premise that such experiments involve the administration of unapproved biological drugs subject to the Agency's IND regulations. Furthermore, in asserting authority to regulate gene therapy experiments, the FDA did something it has so far failed to do with respect to human cloning research: the Agency published an analysis of its legal authority in the Federal Register and invited public comment.[176]

4. Option 4: A Plausible Source of FDA Authority

As just explained, the FDA's gene therapy program rests on the premise that the clinical administration of genetic material to humans requires approval of an IND because it constitutes the administration of an experimental drug. Similarly, the Agency's authority to require advance approval of human cloning experiments depends on the conclusion that such experiments involve the administration of unapproved drugs.

For any clinical experiment to be subject to FDA authority under the FDCA, three conditions must be met. First, the procedure must involve the administration of an "article." Second, that article must fit the Act's definition of "drug" or "device." Finally, the article must be administered to a human subject.[177]

The term "article" appears frequently in the FDCA, usually in conjunction with one of the product categories over which the FDA has been given jurisdiction. For example, the term "drug" includes "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease."[178] "Article," however, is not separately defined.[179] It is comfortable to think of manufactured medical instruments or drug dosage forms, such as pills, tablets, or capsules, as "articles." The FDA,

175. *See id.* at 327–28.

176. *See* Application of Current Statutory Authorities to Human Somatic Cell Therapy Products and Gene Therapy Products, 58 Fed. Reg. 53,248 (Oct. 14, 1993).

177. The Department of Health and Human Services subchapter entitled "Drugs for Human Use" governs clinical investigations of new drugs. Clinical investigations are universally understood to be investigations in human subjects. *See* 21 C.F.R. § 321 (2001).

178. 21 U.S.C. § 321(g)(1)(B) (2000).

179. *See* 21 U.S.C. § 321 (2000).

however, historically has taken a more expansive view. For example, it regulates many computer programs used in the delivery of medical care as devices.[180] Similarly, a gene, alone or combined with an insertion vector such as a virus, may be a "drug."[181] While no court has affirmed this position, neither has it been challenged, and most observers would now consider it firmly established. Thus, in the FDA's view, an "article" need not be man-made; it may be discovered or recovered as well as formulated or constructed.[182] Accordingly, the FDA would be on safe ground contending that the FDCA *could* apply to an experiment that involves the administration of genetic material to a human subject, assuming the experiment's purpose otherwise satisfies FDCA requirements.

In most circumstances, the FDA should have no difficulty satisfying the third condition, i.e., that the article be administered to a human subject. It could be debated whether the cells injected with the prospective clone's genetic material and then transplanted into the surrogate's womb were administered to the "mother" or to the clone. Courts very likely would conclude that this ambiguity was one for the Agency to resolve. However, if an experiment does not involve and is not immediately intended to produce a human being, the FDA lacks jurisdiction.[183]

This conclusion could be a significant qualification. At least initially, many "cloning experiments" will not focus on the ultimate use of a product or material. Rather, they are likely to explore whether a technology is viable for specific applications. Attempts to produce transplantable organs by cloning or to use cloned animals as "factories" for human drugs will aim to create the organ or the animal itself. Human testing of the final product of either application, a clear predicate for FDA jurisdiction, could lie far in the future.

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180. *See* 52 Fed. Reg. 36,104 (Sept. 25, 1987).

181. *See* 58 Fed. Reg. 53,248 (Oct. 14, 1993).

182. *See* Chevron U.S.A., Inc. v. Natural Res. Def. Council, 467 U.S. 837, 844 (1984) (holding that "considerable weight should be accorded to an executive department's construction of a statutory scheme it is entrusted to administer . . . and the principle of deference to administrative interpretations"). *But see id.* at 843 n.9 (stating that the judiciary must reject administrative interpretation in the presence of clear statutory intent).

183. The FDCA only applies if the article or device — or some component, such as a processing agent, preservative, or container — has been, or is intended to be, shipped in interstate commerce. *See* 21 U.S.C. § 360(k) (2000). One can imagine cloning experiments that might escape FDA regulation because of a lack of any interstate element. Even so, the statement in the text could be misleading because the FDA also exercises jurisdiction over the experimental use of new animal drugs under a separate provision of the FDCA. *See* 21 U.S.C. § 360(b) (2000); 21 C.F.R. § 511.1 (2001). Neither the FDA nor anyone else, however, has suggested that this authority could support the Agency's jurisdiction over cloning research.

The second of the three conditions described above requires more extensive analysis. For the FDA to have jurisdiction, the article to be administered must satisfy the FDCA's definition of a "drug" or "device."[184] For simplicity, our discussion continues to focus on the Act's "drug" definition, which, for relevant purposes, encompasses

> (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals . . . .[185]

Both clauses (B) and (C) require an inquiry into the use for which an article is intended. There is considerable case law addressing the concept of "intended use," confirming that it is the seller's intention, *ordinarily* shown by labeling or advertising, that governs.[186] However, the procedures we are imagining are ones for which no labeling has been approved and no advertising has appeared. In such circumstances, it is the research protocol itself that would be consulted to establish what the investigator intends.

We have not seen any protocol prepared by Dr. Seed, but press accounts allow speculation about what he was planning. Apparently, Dr. Seed intended to extract DNA from a human cell (possibly his own), inject that DNA into a donor cell whose DNA had been removed, and then implant the combined material into a surrogate for gestation and eventual birth. The resulting child would be a clone of the individual who donated the original DNA. Assuming this is approximately the procedure Dr. Seed contemplated, we can ask whether it would have fallen within the Agency's drug jurisdiction, as the FDA has claimed.

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184. As previously recounted, the FDA also regulates, through premarket licensure, biological products under PHSA Section 351. *See* 42 U.S.C. § 264 (2000). The Agency has not interpreted § 351 as authorizing it to oversee or restrict clinical research prior to licensure. Rather, the FDA has extended its control of biologics to cloning in order to regulate cloning as a "drug" under the FDCA. *See* Stolberg, *supra* note 92, at A14.

185. 21 U.S.C. § 321(g)(1)(B)–(C) (2000).

186. While the FDA has generally focused on a manufacturer's marketing representations in labeling and advertising to determine an article's "intended use," it has not always limited its inquiry to such explicit materials. In its effort to establish its jurisdiction to regulate cigarettes, for example, the FDA contended that their intended use — to satisfy a craving for nicotine — could be inferred from their physical effects and the manufacturers' awareness of those effects, as evidenced by internal company documents. In ruling that Congress had withheld from the Agency authority to regulate cigarettes, the Supreme Court, per Justice O'Connor, did not find it necessary to rule on the manufacturers' claim that only affirmative public communications could be considered. *See* FDA v. Brown & Williamson Tobacco Corp., 529 U.S. 120 (2000).

There is little doubt that the procedure, if successful, would prove popular even if controversial. Couples who are unable to procreate naturally could use the procedure.[187] In addition, embryos could be cloned through nuclear transfer or embryo splitting to increase the chances of successful conception through more traditional embryo implantation.[188] The procedure appeal especially to couples who risk transmitting hereditary diseases.[189] To suggest, though, that it would therefore fall within the "disease" prong of the FDCA's drug definition would be a stretch. The creation of a new human being would not involve diagnosis or treatment of disease. Perhaps the procedure could be said to involve the prevention of disease if the goal were to produce a child free from a specific disease, e.g., the heritable condition of a potential "parent." But in most cases, disease prevention would be an incidental effect, not a primary purpose. Moreover, the statutory text appears to contemplate an existing person or persons who could be protected against disease by administration of the article in question. In short, the first prong of the drug definition would not seem a plausible source of FDA authority to regulate a procedure whose goal is to create a human being.[190]

The second prong of the FDCA's "drug" definition is a more promising source of FDA authority. The use of cloning technology — indeed any technology — to create a human being could be said to "intend[] to affect the structure or function of the body of man. . . ."[191] Congress almost surely contemplated an *existing* man (or woman) whose body an article might affect. However, its words do not preclude a claim that the implantation of cells in a surrogate in order to clone a child would be intended to affect the body of the resulting clone. In any case, it would be difficult to argue that the procedure was not intended to, or could not be expected to, affect the surrogate's body.[192]

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187. *See* L. Eisenberg, *The Outcome as Cause: Predestination and Human Cloning*, 1 J. MED. & PHIL. 318 (1976).

188. *See* National Advisory Board on Ethics in Reproduction, *Report on Human Cloning Through Embryo Splitting: An Amber Light*, 4 KENNEDY INST. ETHICS J. 251 (1994).

189. *See* JOHN A. ROBERTSON, CHILDREN OF CHOICE: FREEDOM AND THE NEW REPRODUCTIVE TECHNOLOGIES (1994).

190. The possibility that the procedure might *cause* disease in the clone, though certainly of legitimate concern, would not be a basis for FDA jurisdiction. This is not to say that some uses of cloning technology will not yield products over which the FDA would clearly have jurisdiction. For example, there are suggestions that cloning techniques could be used to grow human organs for transplantation or to create herds of genetically engineered animals that could serve as "factories" for medicines. Any experiments to evaluate such products in human volunteers would be subject to the FDA's IND jurisdiction as well as administrative oversight both at the clinical trial stage and, later, when approval for marketing was sought. FDA jurisdiction would not attach, however, until research yielded a product ready for testing in human subjects.

191. 21 U.S.C. § 321(g)(1)(C) (2000).

192. *See* Henkel, *supra* note 137, at 10. The FDA has long, and apparently without

There is convincing evidence that the "structure or function" prong was not designed to encompass all body-affecting articles. Rather, Congress added it in 1938 to enable the FDA to regulate articles that corrected or alleviated bodily conditions not then considered diseases, such as obesity.[193] Thus, to fall within the "structure or function" prong, it could be argued that an article's use must provide some health benefit for the person whose body it is intended to affect. The sponsor of an attempt to clone a human being would surely hope to produce a clone who was healthy, but this result would presumably be a byproduct, not the main objective, of the procedure.

The possible permutations are numerous, and it is not necessary here to determine which experimental applications of cloning technology the FDA could legitimately subject to its requirements. Suffice it to say, the FDCA's "drug" definition does not comfortably encompass *all* of the applications now awaiting investigation.[194] In particular, it is an awkward fit for procedures whose objective is to produce new human beings. This is hardly surprising because Congress could not have foreseen such procedures when it enacted the FDCA. Yet, the FDA's jurisdiction is not confined to products of which Congress was aware in 1938. The FDCA's definitions were drawn in broad terms so that the Agency could regulate new medical technologies and the novel application of old ones.[195]

In defending the FDA's assertion of jurisdiction over tobacco products, Cass Sunstein argued that regulatory agencies possess lawmaking powers as broad as those of a common law court.[196] According to Sunstein, agencies like the FDA should be entitled to extend their statutory authority to reach activities or products whose effects are of the kind they were established to control. This extension of statutory authority is proper despite the fact that Congress could not have anticipated these products or appreciated their effects. Sunstein's thesis

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dispute, exercised jurisdiction over chemical agents that promote conception, presumably on the theory that they are meant to affect the function, if not the structure, of the surrogate. This is not to say that the FDA has asserted jurisdiction over all conception-promoting technologies. To date, the Agency has conspicuously refrained from regulating sperm, ova, or embryos donated to assist reproduction.

193. *See* H.R. REP. NO. 75-2139, at 2 (1938), *reprinted in* 6 A LEGISLATIVE HISTORY OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT AND ITS AMENDMENTS 301 (1979).

194. The reader should not assume that the other statutory categories — "device" and "biological product" — would fill any gaps. The FDA's authority to regulate clinical experiments involving biological products depends on their fitting the FDCA drug definition, and in all relevant respects, the FDCA definition of "device" is similar to the definition of "drug." *See supra* note 118.

195. *See* United States v. Article of Drug Bacto-Unidisk, 394 U.S. 784 (1969); FDA v. Brown & Williamson Tobacco Corp., 529 U.S. 120, 161 (2000) (Breyer, J., dissenting) (citing *Bacto-Unidisk*).

196. *See* Cass R. Sunstein, *Is Tobacco a Drug? Administrative Agencies as Common Law Courts*, 47 DUKE L.J. 1013 (1998).

would support the FDA's authority to regulate human cloning experiments. The safety of such procedures, for the clone and perhaps for the "mother," is surely an open question. Their effectiveness, i.e., their ability to produce a viable human being, is even more uncertain. The chosen instrument of control — requiring advance approval at both the local and national level — is surely a plausible response to such conventional concerns even if the mechanism is not well suited for exploring the deeper ethical and moral issues surrounding the technology.

Professor Sunstein, however, defended the "common law" role of agencies in a quite different procedural context. Though ultimately unsuccessful,[197] the FDA offered a carefully reasoned defense of its position that tobacco products could (and should) be regulated as "drug delivery devices" under the FDCA.[198] Furthermore, before issuing its final regulations, the FDA responded to several thousand comments from interested members of the public, many of whom challenged the Agency's factual and legal premises.[199] In contrast, the FDA has never invited public discussion of the basis or extent of its authority over human cloning research. None of its statements distinguish between scenarios in which Agency jurisdiction may be clear and those in which its authority may be problematic. The result is to leave researchers uncertain about whether planned experiments are legitimately subject to FDA oversight and to inflate the *in terrorem* effect of the Agency's claim of jurisdiction. In short, even if the FDA's legal theory might fit many applications of cloning, there are good reasons to question the procedure that the Agency has followed.

IV. HAS THE FDA VIOLATED THE ADMINISTRATIVE PROCEDURE ACT?

The previous discussion suggests that the FDA's claim that it may regulate some, if not all, cloning experiments under the FDCA's investigational new drug provisions might be upheld. The deference the Agency could expect for its interpretation — in a context where agency regulation is already far-reaching — could defeat any direct judicial challenge. Moreover, it is possible that no facial challenge to the Agency's authority will ever be mounted. Without express permission from the FDA to proceed, few research institutions would be willing to undertake or host experiments that could invite enforcement action. Even

197. *See* FDA v. Brown & Williamson Tobacco Corp., 529 U.S. 120 (2000).

198. *Id.* The FDA's proposed regulations were published in 60 Fed. Reg. 41,314–787, and the final regulations were published in 61 Fed. Reg. 44,619–45,318.

199. For complementary accounts of the FDA's rulemaking process, see the majority and dissenting opinions of Justice O'Connor and Justice Breyer in *FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120 (2000).

if the FDA's jurisdiction is not directly challenged, however, the manner in which the Agency asserted its authority raises separate legal and policy issues.

When a federal agency exercises authority to make law, the APA requires that it give the public notice of its proposal and "give interested persons an opportunity to participate . . . through the submission of written data, views, or arguments."[200] These requirements prevent agencies from engaging in lawmaking without providing notice to those who would be affected by new obligations. Additionally, they allow members of the public to dispute an agency's factual, legal, and policy premises. But the APA also recognizes that not all agency statements about their authority amount to lawmaking. Interpretive rules and statements of agency policy are exempt from its notice and comment requirements.[201] To assess the FDA's conduct in the present context, its statements must first be characterized, an exercise of some difficulty.

In asserting jurisdiction over human cloning experiments, the FDA does not purport to be making new law. It has not issued any document that resembles a rule, interpretive or substantive. The FDA has not published a statement in the Federal Register and does not appear to be contemplating an addition to the Code of Federal Regulations. Yet there can be no question that the FDA's successive statements are intended to alter the legal environment within which cloning research proceeds. The FDA's statements purport to explain requirements already in place, but their practical message to the research community is as emphatic as if Congress had enacted new legislation.

If its procedures were challenged, the FDA would likely argue that its utterances constitute statements of agency policy and thus are exempt from the APA's rulemaking requirements.[202] On this theory, the FDA's statements predict the position that the Agency would adopt in some future formal proceeding. More plausibly in this context, the statements predict the position the FDA would advance in enforcement proceedings against any researcher who undertook a cloning experiment without its approval. In response to a lack of notice claim, the Agency could respond that it was under no obligation to issue any warning at all and could have proceeded to enforce on the premise that the FDCA and agency

200. APA, 5 U.S.C. § 553(c) (2000).

201. APA, 5 U.S.C. § 553(b)(3)(A) (2000). *See generally* Robert A. Anthony, *Interpretive Rules, Policy Statements, Guidances, Manuals, and the Like — Should Federal Agencies Use Them to Bind the Public?*, 41 DUKE L. J. 1311 (1992).

202. *See* 5 U.S.C. § 553(b)(3)(A) (2000) ("General notice of proposed rule making shall be published in the Federal Register, unless persons subject thereto are named and either personally served or otherwise have actual notice thereof in accordance with law. . . . Except when notice or hearing is required by statute, this subsection does not apply: . . . to interpretative rules, general statements of policy, or rules of agency organization, procedure, or practice. . . .").

regulations — IND rules and gene therapy pronouncements — speak for themselves.[203]

One difficulty with this explanation is that the FDA has never acknowledged that its position is contingent or a matter of administrative choice. Rather, the Agency's message, as reflected in Dr. Nightingale's letter and Dr. Zoon's testimony, is that its jurisdiction is unequivocally conferred by statute, and that the conditions for its exercise are already spelled out in its IND regulations. In short, the letter and testimony do not warn about *possible* legal consequences if the facts fit the conditions of the FDA's regulations; they purport to summarize existing, binding legal obligations.

The FDA might argue, in the alternative, that its statements constitute an "interpretive rule" and on this ground are exempt from the APA's rulemaking requirements.[204] This explanation is even more problematic. Interpretive rules customarily are published in the Federal Register, and many issued by the FDA also appear in the Code of Federal Regulations. In addressing cloning, however, the FDA has spurned the Federal Register and has avoided attaching the label "rule" to any of its pronouncements. More to the point, interpretive rules typically purport to explain — that is, to interpret — language found in some indisputably binding statute or regulation. The FDA's only extended discussions of cloning — Dr. Nightingale's letter and Dr. Zoon's testimony — do not refer to any language in the FDCA or the Agency's regulations.

There is another reason to be skeptical of either legal explanation that the FDA might offer for ignoring the APA's rulemaking requirements. For the FDA to acknowledge that its position represented a choice would be to undermine the goal it wished to achieve: forestalling the enactment of new legislation that could impede important medical research. The Agency could not have said "we are prepared to argue that . . ." or "our regulations can be interpreted to fit . . ." and still have expected advocates of legislation to relax their efforts. To fit its strategy, the FDA's statements had to be unequivocal. Moreover, the FDA would not have wished to forfeit the advantages that flow from a belief among those under its authority that its account of the law is not subject to qualification or dependent on context. Statements of agency policy, apparently, are not entitled to *Chevron* deference.[205]

There is authority that would undermine either defense that the FDA might offer for the way it chose to proceed. In *Syncor International*

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203. Of course, the FDA would have to acknowledge that, in any enforcement action, it would have the burden of showing that the researcher's material, and the purpose for which it was used, brought the experiment within the FDCA's ambit.

204. 5 U.S.C. § 553(b)(3)(A) (2000).

205. *See* Christensen v. Harris County, 529 U.S. 576, 587 (2000); *see also* United States v. Mead Corp., 121 S. Ct. 2164, 2174 (2001).

Corp. v. Shalala,[206] the U.S. Court of Appeals for the D.C. Circuit considered a procedural challenge to a 1995 FDA publication, *Regulation of Positron Emission Tomography Radiopharmaceutical Drug Products; Guidance; Public Workshop*. In this publication, which appeared in the "Notices" section of the Federal Register, the FDA announced that positron emission tomography radioactive pharmaceuticals ("PET drugs") were subject to regulation under the FDCA.[207] The notice went on to list sections of the Act that manufacturers of such drugs were obligated to satisfy.[208] Syncor, a manufacturer of PET drugs, sued, contending that the FDA's publication constituted a substantive rule that had not been adopted in accordance with the APA's procedures for rulemaking.[209]

In addressing this challenge, the D.C. Circuit offered an explanation for the distinction between substantive and interpretive rules: "[A]n interpretive rule . . . typically reflects an agency's construction of a statute that has been entrusted to the Agency to administer."[210] In contrast, a substantive rule "*modifies* or *adds* to a legal norm based on the Agency's *own authority*. That authority flows from a congressional delegation to promulgate substantive rules, to engage in supplementary lawmaking."[211]

In applying this distinction, the court first considered whether the FDA had engaged in an interpretive act. It observed: "[The 1995 publication] does not purport to construe any language in a relevant statute or regulation; . . . Instead the FDA's rule uses wording consistent only with the invocation of its general rulemaking authority to extend its regulatory reach."[212] This analysis is illuminating for two reasons. First, it emphasizes that, as the term suggests, "interpretive rules" *interpret* existing laws or regulations. Second, it suggests that when an agency wishes to extend its jurisdictional reach, it must comply with the notice and comment requirements of the APA.[213]

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206. Syncor Int'l Corp. v. Shalala, 127 F.3d 90, 92 (D.C. Cir. 1997).

207. *See id.*; 60 Fed. Reg. 10,594 (Feb. 27, 1995).

208. *Syncor Int'l Corp.*, 127 F.3d at 92–93. These included section 505(i) of the Act , which prescribes conditions for the clinical study of unapproved drugs. *See* 21 U.S.C. § 355(i). These are the same requirements that the FDA has said apply to cloning. 60 Fed. Reg. 10,595 (Feb. 27, 1995).

209. *Synchor Int'l Corp.*, 127 F.3d at 93.

210. *Id.* at 94.

211. *Id.* at 95.

212. *Id.* at 93 (citing *American Mining Cong. v. Mine Safety & Health Admin.*, 995 F.2d 1106, 1112 (D.C. Cir. 1993)). In truth, the FDA notice could be said to represent a determination by the FDA that PET drugs are all within the statutory category of "new drugs" subject to the requirements of section 505, in other words, an "interpretation" of that term. But the notice did not pause to explain this analysis; it merely asserted the Agency's bottom line.

213. *See* Anthony, *supra* note 201, at 1311.

In *Alabama Tissue Center v. Sullivan*,[214] the Seventh Circuit confronted the substantive-interpretive distinction in a challenge to the FDA's claim of authority to regulate transplantable human heart valves. Understanding the court's ultimate ruling requires familiarity with the procedural background of the dispute. In 1980 and 1987, the FDA promulgated sequential rules subjecting what it termed "replacement heart valves" to premarket approval under the Medical Device Amendments to the FDCA.[215] Each rule — the first, classifying the valves in Class III, and the second, calling for the submission of premarket approval applications — was adopted pursuant to the rulemaking requirements of the APA. Producers of mechanical valves and porcine valves participated in both proceedings.[216] Later, in 1990, the FDA announced that the 1980 and 1987 rules also applied to heart allograft valves — i.e., valves recovered from human cadavers. Its declaration to this effect appeared in the "Notices" section of the Federal Register.[217] Six processors of human heart valves challenged both the FDA's jurisdiction over their products and the procedure by which jurisdiction had been asserted.[218] The dispute reached the Seventh Circuit twice.

Initially, the court rejected the tissue banks' challenge.[219] The FDA successfully contended that its notice about heart valve allografts simply interpreted its two existing rules governing "replacement heart valves."[220] In defending this characterization of the FDA's notice, the court emphasized the Agency's own language, which stated that the notice was intended "to *clarify* that replacement heart valve allografts, devices, *are subject to a final rule that was issued by FDA on May 13, 1987*."[221]

The court concluded that the FDA's 1990 explanation was not a new rule requiring premarket approval for human heart valves. Therefore, the court lacked jurisdiction to hear the processors' challenge to the Agency's

214. Alabama Tissue Ctr. v. Sullivan, 975 F.2d 373 (7th Cir. 1992).

215. *Id.* at 375; *see also* Cardiovascular Devices; Classification of Replacement Heart Valves, 45 Fed. Reg. 7948 (Feb. 5, 1980); Cardiovascular Devices; Effective Date of Requirement for Premarket Approval; Replacement Heart Valve, 52 Fed. Reg. 18,162 (May 13, 1987).

216. Classification of Cardiovascular Devices, 44 Fed. Reg. 13,284 (Mar. 9, 1979) (proposed rule); Cardiovascular Devices; Premarket Approval of the Replacement Heart Valve, 51 Fed. Reg. 5296 (Feb. 12, 1986) (proposed rule). No processor of human allograft valves, however, took any notice of the FDA's actions.

217. Cardiovascular Devices; Effective Date of Requirement for Premarket Approval; Replacement Heart Valve Allograft, 56 Fed. Reg. 29,177 (Jun. 26, 1991). In this instance, the FDA's notice did purport to interpret existing regulatory language. The phrase, "replacement heart valves," was surely broad enough to encompass transplantable valves derived from human donors as well as the more familiar valves made from metal or plastic.

218. *Alabama Tissue Ctr.*, 975 F.2d at 376.

219. *See id.* at 374.

220. *See id.* at 377.

221. *Id.*

claim of authority to regulate human tissues as medical devices, implicitly embodied in the Agency's 1987 rule.[222] The heart valve processors had anticipated this possibility and had sued separately in district court. There, the processors' jurisdictional challenge was quickly rejected,[223] sending them back once more to the Seventh Circuit. In *Northwest Tissue Center v. Shalala*, the appellate court reexamined the procedure that the FDA had followed when it asserted jurisdiction over human heart valves.[224] The court ruled that the processors had been deprived of an opportunity to comment on the Agency's determination that human heart valves were subject to regulation as medical devices. Neither of the Agency's earlier proceedings for "replacement heart valves" had provided notice that the resulting rules might apply to allografts.[225] In substance, the Seventh Circuit held that the processors were entitled to advance notice of, and an opportunity to comment on, the FDA's proposed determination that their products were subject to Agency regulation.

The facts in *Syncor* and *Northwest Tissue Center* are similar in important respects to the facts in the situation before us. The two rulings suggest grounds on which one might challenge the FDA's assertion of jurisdiction over human cloning research: the Agency's *ex cathedra* statements that cloning experiments must meet IND requirements arguably amount to a "rule" and are therefore subject to the APA's rulemaking requirements. The FDA's announcement had the immediate effect of subjecting researchers to legal requirements they could not have anticipated, requirements whose violation can carry criminal as well as civil sanctions. It extended Agency jurisdiction into a new arena and imposed new obligations on parties never previously under its control.[226]

Language in a third case supports the reasoning of these cases involving the FDA. In *Appalachian Power Co. v. Environmental*

222. *Id.* at 376–77.

223. *See* Alabama Tissue Ctr. v. Sullivan, 1992 U.S. Dist. LEXIS 17639 (N.D. Ill. 1992).

224. *See* Northwest Tissue Ctr. v. Shalala, 1 F.3d 522, 524 (7th Cir. 1993).

225. *Id.* at 530.

226. In both the PET drugs case and the allograft heart valves case, the FDA argued that its announcement represented a plausible interpretation of existing regulations. In the latter case, for example, the Agency claimed that heart valves recovered from cadavers fell within the category, "replacement heart valves," embraced by its regulations. Yet, it was undeniably true that the Agency had not previously considered allograft valves, or the banks that processed them, subject to its authority. Accordingly, the banks were entitled to claim surprise when the FDA abruptly announced that it was demanding compliance with requirements that the Agency had fashioned without consideration of their applicability to tissue and that were no longer open for public comment. Thus, the flaw in the FDA's reasoning was not its assertion that its statutory authority could extend to allograft valves, but its failure to provide advance notice and an opportunity for the processors to dispute that conclusion or to question the practical consequences that flowed from it. The same can be said of the FDA's sudden assertion of jurisdiction over PET drugs and of its present claim to regulate human cloning research.

Protection Agency,[227] electric power companies challenged a "guidance" document in which the Environmental Protection Agency ("EPA") explained to state agencies the requirements of state-administered permit systems for stationary industrial sources under the Clean Air Act and implementing regulations. The EPA contended that the document was not reviewable because it was not final or binding. This drew the following response from the D.C. Circuit:

> The phenomenon we see in this case is familiar. Congress passes a broadly worded statute. The Agency follows with regulations containing broad language, open-ended phrases, ambiguous standards, and the like. Then as years pass, the Agency issues circulars or guidance or memoranda, explaining, interpreting, defining and often expanding the commands in the regulations. . . . Law is made, without notice and comment, without public participation, and without publication in the Federal Register or the Code of Federal Regulations.
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> . . . If an agency acts as if a document issued at headquarters is controlling in the field, if it treats the document in the same manner as it treats a legislative rule, if it bases enforcement actions on the policies or interpretations formulated in the document, if it leads private parties or State permitting agencies to believe that it will declare permits invalid unless they comply with the terms of the document, then the Agency's document is for all practical purposes "binding."[228]

In his ambitious effort to define the circumstances in which an agency may legitimately elude the APA's requirements for making law, Professor Robert Anthony argued that agencies should provide notice of and invite comment on important new initiatives even when the "interpretive rule" exception might apply.[229] "An agency should endeavor to observe notice-and-comment procedures . . . whenever it contemplates the adoption of an interpretation that would 1) extend the scope of the

227. 208 F.3d 1015 (D.C. Cir. 2000).

228. *Id.* at 1020–21. Similarly, in *Tabb Lakes, Ltd. v. United States*, 715 F. Supp. 726 (E.D. Va. 1988), *aff'd without op.*, 885 F.2d 866 (4th Cir. 1989), the Fourth Circuit set aside, for failure to comply with APA procedures, a Corps of Engineers memorandum interpreting the scope of the Clean Water Act's definition of "navigable waters" in which dredge and fill operations required affirmative permission. The "interpretive" memorandum potentially extended the Corps' permit requirement to millions of new acres over which it had not previously exercised jurisdiction.

229. *See* Anthony, *supra* note 201, at 1373.

jurisdiction the Agency in fact exercises; [or] 2) alter the obligations or liabilities of private parties . . . ."[230]

For many years, the FDA embraced the view advanced by Professor Anthony. In 1977, the Agency incorporated in its own administrative practice regulations a provision promising that it would invite comment before adopting interpretive regulations.[231] The FDA adhered to this commitment when it first undertook to oversee clinical studies of putative genetic therapies in the early 1990s. On three occasions, as it refined its expectations for investigators and sponsors of gene therapy experiments, the FDA publicized its plans in the Federal Register and invited comments from interested members of the public.[232] It is ironic that the Agency dispensed with any similar formalities when claiming authority to regulate human cloning experiments. For, as both Acting Commissioner Friedman and Dr. Zoon have argued, attempts to clone can be viewed as forms of gene therapy, long regulated by the FDA. Yet, the FDA's regulation of gene therapy is the product of an extended public dialogue in which the Agency afforded affected organizations and individual researchers notice of its plans and provided them an opportunity to support, question, or challenge them.

More than a technical legal issue is at stake here. The FDA may claim that all it has done is explain that "experiments to clone a human being" are a form of experimental gene therapy and are therefore subject to the requirements the Agency has long applied to such therapies. The reality, however, is quite different. The FDA's unilateral declarations have not only stifled sponsors and researchers, but have also deflected public discussion of the serious questions surrounding the role, conduct, and oversight of cloning research.[233] None of the Agency's statements say whether its requirements apply only to experiments whose immediate aim is to produce a human clone or encompass any research where results might facilitate the eventual cloning of a human being. They do not detail the safety concerns that ostensibly inspired the Agency to act, nor do they offer guidance to IRBs — the front line of safety — on how to assess those concerns. Furthermore, while the statements acknowledge that there are broader issues surrounding cloning, they offer no hint of how these issues might be addressed in a regulatory process historically concerned primarily with clinical design and patient safety.

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230. *Id.* at 1377.

231. *See* 21 C.F.R. § 10 (1976).

232. *See* Merrill & Javitt, *supra* note 88.

233. Dr. Zoon's testimony before Congress earlier this year was the first time any FDA official had put forward the Agency's claim to jurisdiction in a setting that allowed questions or objections.

V. A NORMATIVE ANALYSIS OF REGULATION OF CLONING RESEARCH

So far, this Article has described the science behind human cloning and examined the possible bases for the FDA's claim of jurisdiction over cloning experiments. Unlike the FDA, however, the authors do not believe that the questions of legal authority can be entirely separated from questions of institutional capacity. This Part examines some of the unique moral and ethical issues any governmental authority must surely confront in regulating cloning research. It also addresses whether the FDA has the qualifications and resources necessary for the task.

A. The Comparative Appeal of FDA Regulation

Despite uncertainty about the Agency's legal authority and reservations about its procedures, plausible arguments can be made for giving the FDA a role in overseeing human cloning research. The FDA administers a regulatory regime whose basic outlines are familiar to medical researchers and whose requirements are already operational. The Agency's assertion of jurisdiction ostensibly provides control of a provocative technology until more finely calibrated requirements can be developed. The FDA regime also allows for flexibility. The basic requirements that researchers must follow are spelled out in agency regulations and supporting guidelines, but research proposals presumably may be considered on an individual basis. Finally, administrative oversight may seem preferable to a very real alternative: a broad legislative ban on all human cloning research.

It is worth recalling that one response to Dolly's birth was a flood of legislative proposals at both the federal and state levels to ban cloning.[234] Multiple bills were introduced in Congress, and a number of state legislatures considered some form of anti-cloning legislation.[235] Though there seemed to be broad agreement that cloning human beings should be forbidden, there was no consensus on legislative details. Many professional and industry groups expressed concern that a broad ban would disrupt or end valuable ongoing genetic research. For them, latent FDA jurisdiction offered an alternative to possibly futile efforts to craft finely-tuned controls through the legislative process.

A major challenge facing advocates of legislation has been their inability to agree on the activities they want to restrict. The term

234. *See, e.g.*, Jennifer Cannon & Michelle Haas, *Recent Developments, The Human Cloning Prohibition Act: Did Congress Go Too Far?*, 35 HARV. J. ON LEGIS. 637, 639–41 (1998).

235. *See generally* NBAC REPORT, *supra* note 27, at 104 (detailing anti-cloning legislation proposed at both the federal and state level).

"cloning" covers a variety of research techniques, including several that have been used beneficially for many years.[236] The experience of the Florida legislature illustrates how a badly drafted law might stifle valuable technology. The Florida legislature was forced to reconsider an enacted cloning statute prohibiting the kind of DNA testing used routinely by law enforcement authorities.[237] Perhaps more importantly, a broadly-worded cloning ban, like one apparently favored by the Bush Administration, would endanger important "stem cell" research, which holds great promise for the development of new medical therapies.[238] Because of such experiences, a diverse coalition of groups, including BIO, PhARMA, and the American Medical Association, have urged legislators to be cautious.

Fashioning a finely-tuned law in this complex area is not an easy task, however. A carefully drawn law that avoids disrupting legitimate applications may be circumvented through technological advances.[239] Consider the experience of the British and Australian legislatures. After adopting cloning bans, they realized that the language of the bans did not even preclude use of the technique that produced Dolly.[240] Thus, any attempt to address the problem legislatively must not only consider the effect a ban would have on beneficial technologies, but must also take into account future technological breakthroughs and new applications of existing techniques.

The technical challenges confronting legislators are compounded by the nature of the cloning debate. The controversy is closely linked to other hotly contested issues of reproductive freedom,[241] which heightens emotions and inhibits reflective deliberation. As a consequence, many legislators, trying to convey a shared sense of moral outrage, hastily drafted bills representing political statements rather than vehicles for exploration and dialogue. Under these circumstances, both the research community and the pharmaceutical industry regarded the ready-made regime offered by the FDA as preferable.

The point here is two-fold. First, there may be advantages to FDA regulation. The implementation of its regulatory regime may discourage

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236. *See* discussion *supra* pp. 7–13.

237. *See* Neil Munro & Marilyn Werber Serafini, *Now a Debate, in Triplicate, Over Cloning*, NAT'L J., Apr. 14, 2001.

238. *See* Rick Weiss, *Bush Backs Broad Ban On Human Cloning*, WASH. POST, June 21, 2001, at A1.

239. *See* Susan Milius, *Science Pokes Loopholes in Cloning Bans*, SCI. NEWS, Feb. 28, 1998 (quoting law professor Lori Andrews as commenting about proposed cloning bans, "[o]nce again, technology may be running circles around the law").

240. *See* Henry T. Greely, *Banning "Human Cloning": A Study in the Difficulties of Defining Science*, 8 S. CAL. INTERDISC. L.J. 131, 136 (1998) (discussing California legislation recounted in the article that managed to cover all proven forms of cloning technology but did not reach certain viable, although untested, cloning techniques).

241. *See* Gianelli, *supra* note 8.

human cloning experiments without the need for new legislation until the safety concerns surrounding human cloning can be addressed. In any case, the FDA's seizure of jurisdiction served the interests of at least two separate groups: those in the research community who feared overbroad legislation, and those in the Clinton Administration who wanted to ensure control over cloning experiments when congressional action seemed unlikely. Their concerns are understandable, but their twin fears — of a legislative ban or of no ban at all — may have caused them to overlook a basic flaw in the solution offered by the FDA. The FDA's intervention not only deflected debate over the content of regulatory controls, it also stifled discussion of the Agency's capacity to assess the most serious issues posed by human cloning.

B. The FDA's Institutional Capacity

An effective regime for regulating cloning must be capable of assessing not only the scientific questions but also the moral and ethical issues. The FDA's exercise of jurisdiction over human cloning research will earn legitimacy only if its processes provide a forum for mediating these issues. It is far from clear, however, that the Agency can fulfill this role.

The FDA's announced plan seems simple: it will apply the procedures it has developed for overseeing the clinical testing of new medicines. These procedures were designed long before cloning and other genetic technologies were realistic possibilities. By announcing that existing law already covers human cloning, however, the FDA has been forced to rely on established procedures rather than to fashion rules specifically to fit this new technology.

1. Medical Concerns

The argument for FDA jurisdiction is strongest when considered in light of the medical concerns raised by the possibility of human cloning. The FDA's regulatory regime is structured to ensure the safety of new medicines before they are administered to human beings. The FDA, and the IRBs on which it relies to help oversee clinical research, are generally capable of addressing the safety of dramatic scientific advances and novel medical applications. By insisting that researchers demonstrate that experiments are not likely to harm subjects, the FDA can help ensure that research does not proceed until there is a high degree of confidence in the technology.[242]

242. *See* NBAC REPORT, *supra* note 27, at 63 ("There is virtually universal concern regarding the current safety of attempting to use [cloning] in human beings.").

While it is not possible to describe all of the hazards that cloning a human being might present, certain risks have been identified. The technology is unreliable and involves high error rates. Dolly was the only living sheep produced in 277 attempts.[243] The risk of fetal and neonatal death, not to mention the dangers to surrogates pregnant with clones, would counsel against any attempt to clone a human being until the success rate is greatly increased.[244] The success rate has reached 10% in experiments on cattle and continues to improve as scientists become more proficient in the use of nuclear transfer technology. But, the frequency of miscarriage and neonatal death is still far too high to justify attempting the procedure in humans.

In addition to the health problems clones and their surrogates might face prior to birth, the complexity of the cell manipulation processes used in cloning raises the possibility that any live child produced could exhibit severe birth or developmental defects.[245] Even Dolly's apparent health is not fully reassuring. Though she seems to be normal, no one really knows Dolly's complete genetic makeup. Defects could be latent but present nonetheless.[246] Indeed, a recent report suggested that Dolly may be showing signs of premature aging, a problem that could reoccur in all clones produced from an adult cell that has already undergone the aging process.[247] Moreover, during later development, Dolly (and other clones) could develop genetic mutations that only emerge as significant problems for their offspring.[248] Until more is known about the survival and longterm health of clones like Dolly, the cloning of a human being has to be viewed as carrying the possibility of significant, if unknown, hazards.[249]

It is precisely such potential hazards that make some administrative oversight reassuring. The FDA's primary responsibility is to protect the public health by ensuring that foods and medical products are safe and, in the latter case, effective as well. The nature of this task is primarily scientific, and FDA officials have the experience to make such judgments. This does not mean that the FDA is fully prepared to address the safety of human cloning. While the Agency has experience with many genetic

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243. *See* Wilmut, *supra* note 2, at 811.

244. *See* Weiss, supra note 78

245. *See* Dan W. Brock, *Cloning Human Beings: An Assessment of the Ethical Issues Pro and Con*, *in* CLONES AND CLONES 141, 157–58 (Martha C. Nussbaum & Cass R. Sunstein eds., 1998).

246. *See* Rick Weiss, *Cloning Suddenly Has the Government's Attention*, INT'L HERALD TRIB., Mar. 7, 1997.

247. *See id*.

248. *See id*.

249. *See id*. (noting the concern of Harold Varmus, director of the NIH, that an old cell used to clone could have developed genetic mutations over the years, leading to a predisposition for certain diseases, such as cancer, in cloned individuals).

technologies, the risks presented by cloning experiments may be unique. In the final analysis, however, questions about the FDA's ability to assess the safety of cloning experiments pale in comparison with doubts about its capacity to grapple with the other issues at the center of the debate.

2. Moral and Ethical Issues

The debate surrounding the announcement of Dolly's birth immediately centered on the moral and ethical issues raised by the possibility of cloning a human being. For many, the ability to clone human beings made possible the previously unthinkable. Such horrific fantasies as armies of identity-less slaves[250] and uncontrolled eugenics experiments[251] emerged as plausible visions of a world in which cloning was permitted. One need not consider these scenarios realistic for cloning to inspire real concerns about the ethics of generating genetic copies of individual human beings. At the most basic level, the prospect of cloned humans raises deep concerns about their status as autonomous individuals, as well as the psychological burdens and identity distortions that cloning might entail.

A central ethical objection is that cloning a human represents "a fundamental threat to the concept and the reality of the human person as a unique and intrinsically valuable entity . . . ."[252] Many philosophers take individuality to be a central concept of the human condition and assert that the creation of identical copies of existing persons is irreconcilable with that concept.[253] The threat that human cloning may present to the concept of individuality was cited time and again in the aftermath of Dolly's birth.[254] In its strongest terms, the idea of individuality is expressed as a natural moral right possessed by every human being, a right that would be violated each time a genetic copy was brought into the world.[255]

This concern for the protection of individuality is not without critics. Many argue that opponents of cloning misunderstand the nature of a cloned individual, who, although sharing another's genetic material,

250. *See* ENZO RUSSO & DAVID COVE, GENETIC ENGINEERING: DREAMS AND NIGHTMARES 158–59 (1998); *see also* ALDOUS HUXLEY, BRAVE NEW WORLD (1932).

251. *See* RUSSO & COVE, *supra* note 250, at 166–76.

252. Laurence H. Tribe, *Technology Assessment and the Fourth Discontinuity: The Limits of Instrumental Rationality*, 46 S. CAL. L. REV. 617, 648 (1973).

253. *See* Leon R. Kass, *The Wisdom of Repugnance*, THE NEW REPUBLIC, June 2, 1997 ("Cloning creates serious issues of identity and individuality.").

254. *See* Brock, *supra* note 245, at 158–61.

255. *See* Ruth Macklin, *Splitting Embryos on the Slippery Slope: Ethics and Public Policy*, 4 KENNEDY INST. OF ETHICS J., 209, 209–26 (1994) (critiquing and exploring this position).

would still be a markedly different person.[256] Even assuming that a clone would be a unique individual, however, his origin could result in other harms. A clone might feel his individuality or sense of self-worth diminished.[257] Awareness of the life choices made by his genetic progenitor could seriously constrict the clone's sense of freedom and convince him that he was fated for a certain destiny. If his progenitor was particularly successful, the clone could feel pressure to live up to that standard, a feeling experienced by many younger siblings but magnified in this instance by genetic identity.[258]

The debate over human cloning also implicates questions about the moral status of clones, which are of more than philosophical interest. Possible uses of cloning include developing specialized organs for transplantation and creating embryos from which scientists can derive beneficial stem cells. If cloned cells are already human, then such an application could be considered immoral because it would amount to creating life for the purpose of destroying it. If cloned cells and cloned embryos are not yet human, however, scientists might legitimately use them for purposes other than the production of human life, such as the use of embryonic cells for the treatment of disease.[259] Recently, for example, a company named Advanced Cell Technology announced that it intends to research cloning for this very purpose, placing the moral status of cloned cells and embryos at the forefront of the cloning debate.[260]

The debate over the moral status of cloned embryos is perhaps most poignant in the area of infertility research. Many advocates of cloning see its potential to relieve otherwise intractable infertility as the strongest argument for further research.[261] However, given the technology's imperfections, early efforts to clone a human being will almost certainly entail a significant risk of miscarriage and the destruction of a number of embryos.[262] These potential consequences are just one example of the difficult choices facing policymakers.

Both commentators and politicians have cited these moral and ethical concerns, as well as the potential harms to clones themselves, as a basis for favoring an outright ban on human cloning experiments. An outright ban is a superficially appealing response and, perhaps more importantly,

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256. *See* Stephen Jay Gould, *Dolly's Fashion and Louis's Passion: Ruminations on the Downfall of a King and the Cloning of a Sheep*, 106 NAT. HIST. 18, 21–22 (1997).

257. *See* Brock, *supra* note 245, at 159.

258. *See* John D. Rainer, *Commentary*, *in* 3 MAN AND MED.: J. VALUES & ETHICS IN HEALTH CARE 115, 116 (1978).

259. *See* Rick Weiss, *Firm Aims to Clone Embryos for Stem Cells*, WASH. POST, July 12, 2001, at A1.

260. *See id*.

261. *See* John A. Robertson, *Liberty, Identity, and Human Cloning*, 76 TEX. L. REV. 1371, 1378–80 (1998).

262. *See* Brock, *supra* note 245, at 157–58.

a politically expedient one in a country where 90% of those polled believe that cloning is morally wrong.[263] This broad opposition may have influenced the Clinton Administration's decision to establish a de facto moratorium through the assertion of FDA regulatory authority. However, calls for a total ban on cloning experiments fail to recognize the complexity of the debate.[264] When one appreciates the range of issues that must be addressed, the limitations of the FDA's regulatory regime are exposed.

C. Limitations of the FDA's IND Regime

The FDA bases its jurisdiction on the FDCA provision that gives the Agency authority to approve any shipment — and thus almost any administration — of an investigational new drug. The provision in question, section 505(i) of the FDCA, directs the FDA to establish regulations for exempting "drugs intended solely for investigational use by experts" from the Act's general prohibition against the shipment of unapproved drugs.[265] Section 505(i) specifies that the Agency's regulations shall require the submission of preclinical studies, the investigator's assurance of supervision, and the maintenance of records and submission of reports to enable the FDA to evaluate the drug's safety and effectiveness.[266] It also directs the FDA to require investigators to inform research subjects that the drug is being administered for investigational purposes and to secure their consent to participate.[267] The primary aims of this provision are to protect the safety and autonomy of subjects and to assure that the FDA has access, both while studies are underway and after they have concluded, to all evidence relevant to assessing a drug's safety and effectiveness.

Section 505(i) authorizes the FDA to impose other conditions on obtaining an IND exemption that are "related to the protection of the public health."[268] Pursuant to this authority, and the specific directives just summarized, the FDA has adopted progressively more elaborate IND requirements.[269] Among the most important is the requirement that any

263. A Time/CNN poll conducted in February 2001 shows that 90% of respondents believed that it was a "bad idea" to clone a human being, while 67% of respondents believed that it was a "bad idea" to clone animals such as sheep. *See* Time/CNN Poll — Cloning, *at* http://www.time.com/time/health/printout/0,8816,99005,00.html (last visited Oct. 11, 2001).

264. *See* Richard Dawkins, *What's Wrong with Cloning?*, *in* CLONES AND CLONES 54 (Martha C. Nussbaum & Cass R. Sunstein eds., 1998).

265. FDCA § 505(i)(1), 21 U.S.C. § 355(i) (2000).

266. *Id*.

267. *See* 21 U.S.C. § 355(i)(4).

268. 21 U.S.C. § 355(i)(1).

269. *See* Investigational New Drug Application, 21 C.F.R. § 312 (2001).

study be reviewed by a qualified institutional review board.[270] An IRB's primary responsibility is to protect the safety and assure the informed consent of study participants. IRBs are not directed to assess whether a study is morally acceptable or socially beneficial. Nor is the FDA. One could perhaps construe some of the FDA's regulations as authorizing agency reviewers, or an IRB, to explore the ethical questions presented by a proposed study. However, doing so would go beyond the statute's central concern for subject safety and autonomy, and there is little evidence that such issues are raised by, or explored in reviewing, typical INDs.

The FDA has shown little desire to confront the ethical and moral questions about cloning. Ms. Holston's 1998 letter to Senator Kennedy implied that the Agency saw its role as limited to evaluating the safety of proposed experiments.[271] Dr. Zoon, in her congressional testimony, was even more forthright. In response to questions from members of the committee, she acknowledged that if the Agency were persuaded that an experiment presented no "safety concerns" — whatever that might mean — its responsibility would be at an end.[272] Yet, it seems unlikely that, when confronted with a proposed experiment, Agency officials could ignore the broader issues — issues that the Agency has neither the legal mandate nor the experience and expertise to resolve.

If the FDA were determined to confine its own review to the immediate safety of study participants, it would face pressure to arrange for another forum in which the broader issues raised by cloning research could be debated. No such forum has been legally chartered. The RAC has statutory authority to review proposed studies that have the requisite link to federal funding, but its jurisdiction does not extend to studies sponsored by the private sector. And President Clinton's directive to federal funding agencies and research institutions effectively assures that for the foreseeable future the only research into human cloning carried out in this country will be privately supported.[273]

The importance of debate over cloning conflicts with another feature of the FDA's traditional regulation of clinical research. The FDA's review of proposed clinical studies typically occurs outside of public view. This is necessary to protect the confidentiality of sponsors' proprietary information. Most new therapies are developed by for-profit firms that are aiming at commercial markets, and any oversight process should protect their proprietary rights. This same reasoning would apply to proposed cloning experiments sponsored by commercial firms. Thus,

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270. *See* Institutional Review Boards, 21 C.F.R. § 56 (2001).
271. *See* Holston, *supra* note 90.
272. Zoon Testimony, *supra* note 17, at 90.
273. *See supra* note 6 and accompanying text.

reposing oversight responsibility exclusively in the FDA would not only fail to facilitate, but may even stifle, public debate about cloning.

The FDA has confronted this dilemma in its regulation of gene therapy. Some of the research protocols submitted to the Agency in the form of IND applications have raised questions that demand more than the traditional assessments of patient safety, clinical promise, and confirmation of informed consent. They have raised issues, if not of ethics, at least of appropriateness. The FDA has sometimes found it convenient to direct debate over such issues to the RAC.[274] This collaboration, however, raises its own difficulties. First, because the RAC insists on meeting in open session, the two agencies have been struggling to fashion special procedures for handling the confidential information in IND applications.[275] Second, by ceding responsibility for evaluating the non-scientific issues raised by proposed studies, the FDA has essentially acknowledged its inability to assess the kinds of issues that cloning dramatizes.

D. An Alternative Approach

The joint oversight of gene therapy experiments described above illustrates a context in which the FDA, persuaded that it was not equipped to deal with the ethical and social implications of a technology, acknowledged an alternative forum for discussion of those issues. The gene therapy experience has exposed the limitations of this model, however, and the difficulties the FDA and the RAC have encountered would undoubtedly be multiplied in the context of human cloning. The accelerating pace of scientific discovery may require a more radical rethinking of the regulatory landscape. Great Britain's attempt to grapple with the moral and ethical issues surrounding human cloning, and the regulatory approach it has adopted, provide a model to compare with the FDA's response.

Unlike their U.S. counterparts, legislators in Great Britain were not writing on a clean slate when they first confronted the possibility of human cloning. In 1990, Parliament passed the Human Fertilisation and Embryology Act ("HFEA").[276] The purpose was to provide stringent controls over embryo research.[277] In fashioning this legislation Parliament had the foresight to address the potentially troubling uses of

274. *See* Merrill & Javitt, *supra* note 88, at 325.

275. *See* Availability for Public Disclosure and Submission to FDA for Public Disclosure of Certain Data and Information Related to Human Gene Therapy or Xenotransplantation, 66 Fed. Reg. 4,688 (proposed Jan. 18, 2001) (to be codified at 21 C.F.R. pts. 20, 312, 601); *Gene Therapy Data Must Not Be Declared Proprietary*, THE BLUE SHEET, Feb. 28, 2001, at 9.

276. Human Fertilisation and Embryology Act, 1990, c. 37 (Eng.) [hereinafter HFEA].

277. *See id*.

cloning technology. Section 3 of the HFEA expressly banned the use of nuclear transfer technology to clone a human being.[278] Thus, a decade ago, Great Britain had already accomplished what U.S. policymakers are still struggling to achieve — an express ban on attempts to clone a human being.

In addition to banning the use of nuclear transfer technology to clone a human being, the HFEA established the Human Fertilisation and Embryology Authority (the "Authority"),[279] which regulates, licenses, and collects data on fertility treatments and human embryo research in the United Kingdom.[280] The Authority consists of twenty-one members who are appointed by the United Kingdom Health Ministers.[281] The Act requires that Members be selected not because they represent any particular organization or group, but rather for their personal knowledge and expertise.[282] To ensure a variety of perspectives, more than half of the Authority's membership must come from disciplines outside of medicine and human embryo research.[283] The Authority is structured to consider the key ethical issues surrounding new genetic or reproductive technologies in the context of the national debate that such advances may cause.

Although the Authority seems well-equipped to address the ethical, moral, and scientific issues raised by cloning technologies, the Blair government also formed a second organization whose institutional mission brought it into the center of the cloning debate. The Human

278. *See id.* § 3(1) ("No person shall — (a) bring about the creation of an embryo; or (b) keep or use an embryo, except in pursuance of a licence.").

279. *See id.* § 5(1)–(2)(b) (stating that "[t]here shall be a body corporate called the Human Fertilisation and Embryology Authority" which is to consist of "a chairman and deputy chairman" and "such number of other members as the Secretary of State appoints").

280. "The HFEA's principal task is to regulate, by means of a licensing system, any research or treatment which involves the creation, keeping and use of human embryos outside the body, or in the storage or donation of human eggs or sperm." HUMAN FERTILISATION & EMBRYOLOGY AUTH., CODE OF PRACTICE 5 (4th ed. 1998).

281. *See* Ruth Deech, Chairman's Welcome, *at* http://www.hfea.gov.uk/main.htm (last visited Oct. 11, 2001).

282. *See* HFEA, *supra* note 279, at Schedule 1, § 4(1)–(4), *available at* http://www.hmso.gov.uk/acts/acts1990/Ukpga_199900037_en_1.htm (last visited Oct. 11, 2001). In a section detailing the Authority's membership, the Chairman of the Authority states: "In order that a perspective can be maintained which is independent of the medical-scientific view, the HFE Act requires that the Chairman, Deputy Chairman and at least half of the HFEA's Membership are neither doctors [n]or scientists involved in human embryo research or providing infertility treatment. Members are not appointed as representatives of different groups, but bring to the HFEA a broad range of expertise: medical, scientific, social, legal, managerial, religious, and philosophical." HUMAN FERTILISATION & EMBRYOLOGY AUTH., NINTH ANNUAL REPORT & ACCOUNTS 1 (2000), *available at* http://www.hfea.gov.uk/annrep2000/annrep%202000a.pdf (last visited Oct. 11, 2001).

283. *See* HFEA, *supra* note 279, at Schedule 1, § 4(4).

Genetics Advisory Commission (the "Commission"), which was operational from December 1996 through December 1999,[284] was created to provide unbiased advice on issues arising from genetic technologies. Specifically, the Commission's charge was: (1) "to keep under review scientific progress at the frontiers of human genetics and related fields"; (2) "to report on issues arising from new developments in human genetics that can be expected to have wider social, ethical, and/or economic consequences"; and (3) "to advise on ways to build public confidence in, and understanding of, the new genetics."[285]

Thus, in contrast to the U.S. government, which seemed ill-prepared for Dolly's birth, Great Britain had already created the institutional machinery to address the issues presented by the possibility of human cloning. Instead of having to deputize an agency whose experience poorly equips it to grapple with many of the issues surrounding human cloning, Great Britain could turn to established entities whose authority made them natural candidates to take a leading role in fashioning controls for this new technology. On the heels of the Roslin Institute's announcement, the Blair government asked the Commission and the Authority to prepare a joint report addressing the issues presented by advances in cloning technology and recommending actions that should be taken in response.

The Authority and the Commission promptly formed a working group consisting of members of both entities.[286] The working group developed a consultation paper that outlined the issues raised by the national debate and the existing regulatory framework.[287] This framework included a narrow ban that would prevent attempts to reproduce a human being through cloning but would not obstruct experiments into possible therapeutic uses of cloning technologies.[288] The consultation paper was widely distributed through the national media and was made available on a government web site.[289]

Release of the working group's consultation paper opened a three month period for comment by members of the public.[290] In addition, the

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284. In December 1999, the Human Genetics Advisory Commission was superseded by the Human Genetics Commission. Information about the Human Genetics Commission can be found at http://www.hgc.gov.uk.

285. HUMAN GENETICS ADVISORY COMM'N, TERMS OF REFERENCE, *at* http://www.dti.gov.uk/hgac/comm.htm (last visited Oct. 11, 2001).

286. *See* HUMAN GENETICS ADVISORY COMM'N, CLONING ISSUES IN REPRODUCTION, SCIENCE & MEDICINE § 1.9 (Dec. 1998), *available at* http://www.dti.gov.uk/hgac/papers/papers_d.htm (last visited Oct. 11, 2001).

287. *See* HUMAN GENETICS ADVISORY COMM'N, CLONING ISSUES IN REPRODUCTION, SCIENCE & MEDICINE (Jan. 1998), *available at* http://www.dti.gov.uk/hgac/papers/papers_c.htm (last visited Oct. 11, 2001).

288. *See id*.

289. *See* HUMAN GENETICS ADVISORY COMM'N, *supra* note 286, § 2.1.

290. *See id.* § 1.11.

working group actively sought the opinions of scientists, philosophers, religious leaders, and ethicists. During the public comment period, interested groups throughout the United Kingdom held public forums at which participants discussed the issues surrounding cloning and then submitted the results of these discussions to the working group. By the end of the comment period, the working group had received nearly 200 comments.[291]

In December 1998, the Authority and the Commission issued a joint report entitled "Cloning Issues in Reproduction, Science, and Medicine."[292] The group reported a broad consensus among the comments that cloning should not be used for reproductive purposes. Since this sentiment matched the working group's own preferred approach, it recommended that the Authority adhere to its previously announced plan to refuse all license requests for experiments concerning reproductive cloning.[293] More significantly, the working group stated that the existing ban on the use of nuclear transfer technology to produce a human being was sufficient to make any attempt to clone a human being a crime.[294] At the same time, the working group recommended that the government consider legislation explicitly banning human cloning through the use of any technique.[295]

Although it squarely opposed any use of cloning technologies for reproductive purposes, the working group drew a clear distinction between "reproductive" cloning and "therapeutic" cloning.[296] Its report affirmed that certain uses of cloning technology held great promise for the treatment of illness and disease, and it recommended that legislation not threaten these potential benefits.[297] The working group recommended that the Authority be permitted to license embryo research involving cloning technologies in two specific areas: the development of therapies for treatment of mitochondrial diseases and the development of therapies for diseased or damaged tissues or organs.[298]

In response to the joint working group's recommendation to expand the purposes for which human embryos could be used in research, the Blair government asked the country's Chief Medical Officer, Liam Donaldson, to form an expert advisory commission to consider the joint working group's recommendations.[299] The expert advisory commission

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291. *See id.* § 2.3.
292. *See id*.
293. *See id.* § 9.2.
294. *See id*.
295. *See id*.
296. *See id.* § 5.1.
297. *See id.* § 9.3.
298. *See id*.
299. *See* Liam Donaldson, CMO's Letter on the Expert Advisory Group on Therapeutic Cloning in Humans, *available at* http://www.doh.gov.uk/cegc/cmolet.htm

was formed because the Blair government wanted "to establish the extent to which there is an identified need for and interest in research on human embryos and involving cloning techniques for therapeutic purposes."[300] Dr. Donaldson was asked "to seek views widely on these questions and to establish more clearly the evidence of potential benefits for human health of such research."[301]

On August 16, 2000, Dr. Donaldson and his advisors published their report.[302] They announced that, because therapeutic cloning technologies held such promise for the treatment of disease, they recommended that the government permit the use of human embryos in cloning research provided that those embryos were destroyed within fourteen days of their creation.[303] At the same time, they urged the government to maintain its ban on any use of reproductive cloning and to enact new legislation expressly forbidding any cloning technique designed for reproductive purposes.[304] Thus the Donaldson commission echoed the earlier working group's conclusion that reproductive cloning should be banned, but that therapeutic uses of the technology should not.

The Blair government accepted the expert advisory commission's recommendations and forwarded them to Parliament,[305] which voted overwhelmingly to expand human embryo research.[306] This Article is not immediately concerned with the conclusions reached by the British deliberative bodies or their ultimate political fate, however. Rather, the British government's approach to the challenge of human cloning merits study because it contrasts, in both its public character and thoroughness,

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(last visited Oct. 11, 2001).

300. *Id.*

301. *Id.*

302. *See* DEPT. OF HEALTH, STEM CELL RESEARCH: MEDICAL PROGRESS WITH RESPONSIBILITY (June 2000), *available at* http://www.doh.gov.uk/cegc/stemcellreport.pdf (last visited Oct. 11, 2001).

303. *See id.* § 5.10, at 45.

304. *See id.* § 5.10, at 47.

305. The British Government issued a response stating that it "accepts the Report's recommendations in full and will bring forward legislation where necessary to implement them as soon as the Parliamentary timetable allows." SECRETARY OF STATE FOR HEALTH, GOVERNMENT RESPONSE TO THE RECOMMENDATIONS MADE IN THE CHIEF MEDICAL OFFICER'S EXPERT GROUP REPORT "STEM CELL RESEARCH: MEDICAL PROGRESS WITH RESPONSIBILITY" 1 (Aug. 2000), *available at* http://www.doh.gov.uk/cegc/cm4833.pdf (last visited Oct. 11, 2001).

306. *See UK to Extend Embryo Research*, BBC NEWS, Dec. 19, 2000, *at* http://news.bbc.co.uk/ hi/english/sci/tech/newsid_1078000/1078672.stm (last visited Oct. 15, 2001). This law is now being challenged in court by anti-abortion activists, who fear that a loophole in the law will allow scientists to create cloned babies. *See Embryo Cloning Faces Court Challenge*, CNN, Jan. 26, 2001, *at* http://www.cnn.com/2001/WORLD/ europe/UK/01/26/cloning/index.htm (last visited Oct. 15, 2001).

with the defensive approach adopted by the Clinton and Bush Administrations.

While both governments recognized the need to reconcile the public's moral and ethical apprehensions with the potential scientific and therapeutic benefits that cloning may offer, their approaches differed sharply. First, although Parliament will make the important decisions regarding the extent to which cloning research is permitted in Great Britain, the question was first presented to bodies structured to address the difficult issues raised by new genetic technologies. Second, through the composition of the Authority, professionals with expertise in philosophy and ethics were represented in the policy development process, which was not left to experts in the medical and scientific fields. Third, the processes of the working group gave interested parties, and the public, opportunities to contribute to the debate. In these key respects, Britain has pursued a more open and democratic process for developing national policy on cloning research.

Our critique of the FDA's assertion of authority is not intended to be a general indictment of the U.S. government's reaction to the public clamor following the announcement of Dolly's birth. President Clinton did promptly ask the NBAC to conduct a broad-based inquiry into the scientific, moral, ethical, and religious aspects of the issue.[307] The NBAC went to some lengths to solicit input from a variety of perspectives.[308] This is the kind of "public" discussion we advocate. Moreover, the NBAC report's recommendation of a temporary moratorium on human cloning experiments was designed to ensure time for further discussion of the issue.[309] The report specifically stated that any legislation should include a sunset provision so that Congress would be forced to revisit the issue after a specified period of time to determine whether a ban on human cloning experiments was still necessary.[310]

The NBAC's handling of its task, and its recommendations, reflected a laudable concern for public discussion of the important issues surrounding human cloning research. Recognizing that public attitudes toward human cloning research were varied and sharply divided, the NBAC recommended that:

> [t]he federal government, and all interested and concerned parties, encourage widespread and continuing deliberation

307. *See Clinton Urges Ban on Cloning of Humans*, CHRISTIAN CENTURY, June 18, 1997, at 583.

308. *See* NBAC REPORT, *supra* note 27, at i–v.

309. *See id.* at 109 ("It is critical, however, that such legislation include a sunset clause to ensure that Congress will review the issue after a specified time period (three to five years) in order to decide whether the prohibition continues to be needed.").

310. *See id.*

> on these issues in order to further our understanding of the ethical and social implications of this technology and to enable society to produce appropriate long-term policies regarding this technology should the time come when present concerns about safety have been addressed.[311]

In addition to encouraging "widespread and continuing deliberation" on the issue of human cloning, the NBAC also recommended that:

> because scientific knowledge is essential for all citizens to participate in a full and informed fashion in the governance of our complex society . . . Federal departments and agencies concerned with science should cooperate in seeking out and supporting opportunities to provide information and education to the public in the area of genetics, and on other developments in the biomedical sciences, especially where these affect important cultural practices, values, and beliefs.[312]

Thus, the NBAC believed that an agency can properly address advances in genetic technology, such as human cloning, only if it can educate the public about the scientific, moral, and ethical issues involved and to encourage public discussion about those issues.

In offering its recommendations, the NBAC recognized that the debate over human cloning involved complicated moral and ethical questions about which no consensus existed. The NBAC contemplated wide-ranging discussion of the issues surrounding human cloning so that "appropriate long-term policies" could be designed.[313] This approach is preferable to the outright ban adopted in Japan and France[314] and supported by the Bush Administration here.[315] It is our fear, however, that the FDA's assertion of jurisdiction, accompanied by statements that no human cloning experiments may proceed without its approval, has stifled the very debate envisioned by the NBAC.

The initial reactions of the Bush Administration to the problem of human cloning — which combines at least tacit support for the FDA's ban on human cloning with support for broad anti-cloning legislation[316] — similarly seems unlikely to produce the kind of wide-

311. *Id.* at 110.
312. *Id.*
313. *See id.*
314. *See France Forbids Human Cloning*, CNN, June 20, 2001, *at* http://www.cnn.com/2001/WORLD/europe/06/20/france.cloning (last visited Oct. 12, 2001).
315. *See* Weiss, *supra* note 238, at A1.
316. *See id.*

ranging debate and consideration of creative approaches exhibited in Great Britain. This is unfortunate. The debate over human cloning (as well as the related issue of stem cell research[317]) involves questions of great complexity. Policymakers must balance the potential for important medical benefits against the widespread moral and ethical aversion to these new technologies. If a specialized regulatory regime cannot be designed for these cutting-edge genetic technologies, the United States may well continue to seek quick political solutions that neither encourage debate nor account for the complexity of the questions involved.[318]

In comparing the respective approaches of the American and British governments, we must not overlook an important difference between the two political systems. As the elected (now re-elected) leader of a parliamentary majority, Prime Minister Blair was and is in a position to control the legislative agenda and, within broad limits, to assure the enactment of legislation that his government supported and drafted. President Clinton, by contrast, had to compete for attention from a Congress controlled by the opposing party and surely knew that any legislation his administration crafted might be eviscerated in the legislative process. This fundamental difference between the two systems may help explain why the Clinton Administration rather quickly withdrew from the legislative arena and searched for an administrative, ostensibly interim, response to the challenge of human cloning.

We are, nonetheless, struck by the contrast between the two countries' responses to the prospect of human cloning. While Great Britain's approach encouraged public debate, the FDA's peremptory assertion of jurisdiction cut short public discussion and channeled into a closed regulatory process decisions about which experiments, if any, to allow. None of the important moral and ethical questions surrounding human cloning have been addressed, much less resolved, by the FDA's bare claim of jurisdiction. Little in the Agency's practice or experience warrants confidence that these issues will be adequately explored in the IND process.

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317. *See Selling Cells*, PHILA. INQUIRER, July 12, 2001, at A16; *Stem Cell Impasse*, WASH. POST, July 12, 2001, at A26; *Stem Cells: Abortion Politics Aside, Bush Shouldn't Bar Research*, HOUSTON CHRON., July 11, 2001, at A24; *Stem Cells and Life, Part 2*, CHI. TRIB., July 12, 2001, § 1, at 26.

318. In an interview with *Salon*, Dr. Wilmut expressed concern that an ill-considered cloning ban could put an end to valuable genetic research before the implications of the technology were fully explored and understood. Dr. Wilmut stated: "I totally understand that people find this sort of research offensive, and I respect their views. It's also possible for a minority to have a very large influence. Now if society says it doesn't want us to do this kind of research, well, that's fine. But I think it has to be an overall view by an informed population." Andrew Ross, *Dr. Frankenstein, I Presume*, SALON (1997), *at* http://www.salon.com/feb97/news/news2970224.html (last visited Oct. 11, 2001).

VI. CONCLUSION

We are not the first to question the FDA's credentials for the task it has casually assumed. In November 1998, a few weeks after distribution of Dr. Nightingale's letter,[319] a biotechnology newsletter reported on a speech by Dr. David Kessler, Dean of Medicine at Yale University and the former FDA Commissioner.[320] According to the report, Dr. Kessler expressed no doubts about the FDA's legal authority to regulate cloning research, but argued that the Agency "lacks the regulatory framework and the resources to prevent the cloning of a human and other potentially unethical or unsafe biomedical experiments."[321] In an interview following his speech, Dr. Kessler observed, "There is a difference between saying you have jurisdiction and knowing how to do it thoughtfully . . . . There is no question that under the law FDA can regulate cloning. The question is, does the Agency know how to regulate it and does it have the resources to do so?"[322]

Perhaps the only clear message that emerges from the debate over human cloning is that there are no simple solutions. The science is complex and rapidly evolving, and it continues to raise questions that our society seems ill-equipped to answer. The public debate may have focused on an improbable parade of horribles, but the fundamental issues at stake are real. Concerns about the risks of human cloning and the moral issues that it raises are not going to go away. Neither, however, will the advocates of scientific progress, who will properly continue to point to the potential benefits that human cloning offers.

The FDA's assertion of regulatory authority provides some assurance that morally troubling experiments will not proceed without some governmental review. The Agency's ability to deploy an existing system of oversight may comfort critics of the technology and at the same time reassure those who worry that Congress might hastily enact restrictions that would impede scientific inquiry. However, we question whether FDA jurisdiction is the best vehicle for fashioning a long-term policy for addressing the unique concerns generated by advances in genetic technology and the potential for human cloning.

Recently, the magazines *Time*[323] and *Wired*[324] dedicated their covers, and many pages within, to the startling news that human cloning may soon be a reality. Both magazines detailed the relative ease with which

319. *See supra* note 15 and accompanying text.

320. *See* Steve Usdin, *Kessler's Doubts*, BIOCENTURY: THE BERNSTEIN REPORT ON BIOBUSINESS, Nov. 16, 1998, at A1.

321. *Id.*

322. *Id.*

323. *See* Arthur Hochstein & Lon Tweeters, *Baby, It's You! And You, and You . . .*, TIME, Feb. 19, 2001, at 46.

324. *See* Brian Alexander, *(You)*^{2}, WIRED, Feb. 2001, at 120.

cloning can now be done and quoted unnamed sources in the scientific community who insisted that a human would be cloned within the next few years. In the words of Delores Lamb, an infertility expert at Baylor University, "[i]t's inevitable that someone will try [to clone a human being], and someone will succeed."[325] If this speculation is accurate — and we have no reason to think that it is not — the FDA's regulatory structure will confront increased pressures, very possibly in the form of the successful cloning experiment that evaded agency review.

The tension between science and morality that human cloning exposes is not new, nor is the challenge to our legal structure that technological advance presents. But the accelerating pace of scientific advance presents unprecedented challenges for policymakers and citizens alike. The debate over cloning demonstrates that novel technologies are not easily regulated under a statute drafted many decades ago. More importantly, the debate illustrates that possibilities once believed unthinkable inevitably strain our ability to formulate wise public policy. In this sense, the ultimate impact of the FDA's assertion of jurisdiction may be to inhibit creative legislative and regulatory solutions to a problem that admits of no easy answers.

325. Hochstein & Tweeters, *supra* note 322, at 48.